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Please search Figure 1 with protein databases.
Also search CSF-1hr, CSF-1en & CSF-G

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Prema Mertz

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CLUSTER NAME      CLUSTER DEFINITION
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.BIO              MEDLINE HCAPLUS EMBASE BIOSIS WPIDS IFIPAT
                  BIOTECHDS DISSABS CONFSCI LIFESCI SCISEARCH JAPIO
                  JICST-EPLUS

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                KAUFMAN, R? OR KAUFMAN R? OR WONG,G? OR WONG, G? OR WONG
                G? OR WANG,E? OR WANG, E? OR WANG E?)/AU,IN
L2              QUE  L1 AND CSF
L3              QUE  L2 AND (CSF ILE# OR CSF THR OR CSF G)


F1          13*  MEDLINE
F2          12*  EMBASE
F3          12*  BIOSIS
F4           7   HCAPLUS
F5           6*  LIFESCI
F6           2   WPIDS
F7           2*  SCISEARCH


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                G? OR WANG,E? OR WANG, E? OR WANG E?)/AU,IN
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L3              QUE  L2 AND (CSF ILE# OR CSF THR OR CSF G)
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L11          54 SEA L3
L12          16 DUP REM L11 (38 DUPLICATES REMOVED)
L13          16 SOR L12 PY
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L13 ANSWER 1 OF 16 WPIDS COPYRIGHT 1996 DERWENT INFORMATION LTD
AN 86-042122 [06] WPIDS
DNC C86-017927
TI Recombinant colony stimulating factor protein - used for treating infection or granulocytopenia or activating neutrophils in animals.
DC B04 D16
IN **CLARK, S C**; **KAUFMAN, R J**; **WANG, E A**; **WONG, G G**; **KAUFMAN, R**; **WANG, E**; **WONG, G**
PA (SANO) SANDOZ AG; (CLAR-I) CLARK S C
CYC 25
PI WO8600639 A 860130 (8606)* EN 91 pp
RW: AT BE CH DE FR GB IT LU NL SE
W: AU DK FI HU JP KR NO SU US
AU8545456 A 860210 (8619)
PT--80776 A 860421 (8619)
NO8600775 A 860512 (8626)
EP-188479 A 860730 (8631) EN
R: AT BE CH DE FR GB IT LI LU NL SE
HU--38675 T 860630 (8633)
FI8600308 A 860122 (8647)
JP61502682 W 861120 (8701)
ZA8505102 A 870105 (8712)
ES8701226 A 870216 (8714)
DK8601028 A 860306 (8725)
EP-337359 A 891018 (8942) EN
R: AT BE CH DE FR GB IT LI LU NL SE
AU8940090 A 891207 (9004)
AU9054976 A 900913 (9044)
EP-188479 B 910911 (9137)
R: AT BE CH DE FR GB IT LI LU NL SE
DE3584089 G 911017 (9143)
IL--75725 A 930221 (9314)
DK9300594 A 930521 (9337)
IL--94754 A 930922 (9349)
AU-644359 B 931209 (9405)
HU-208711 B 931228 (9405)
DK-168709 B 940524 (9424)
JP06199897 A 940719 (9433) 26 pp
NO9403300 A 860313 (9443)
JP06319557 A 941122 (9506) 27 pp
JP07163351 A 950627 (9534) 28 pp
ADT WO8600639 A 85WO-EP00326 850704; EP-188479 A 85EP-0903275 850704; JP61502682 W 85JP-0503011 850704; ZA8505102 A 85ZA-0005102 850705; ES8701226 A 85ES-0544868 850704; EP-337359 A 89EP-0106339 ; IL--75725 A 85IL-0075725 850704; DK9300594 A Div ex 86DK-0001028 850704, 93DK-0000594 930521; IL--94754 A 85IL-0094754 850704; AU-644359 B 90AU-0054976 900514, Div ex 85AU-0045456 ; HU-208711 B 85HU-0003131 850704, 85WO-EP00326 850704; DK-168709 B 85WO-EP00326 850704, 86DK-0001028 860306; JP06199897 A Div ex 85JP-0503011 850704, 93JP-0175978 850704; NO9403300 A 85WO-EP00326 850704, Div ex 86NO-0000775 860303, 94NO-0003300 940907; JP06319557 A Div ex 85JP-0503011 850704, 93JP-0176039 850704; JP07163351 A Div ex 85JP-0503011 850704, 94JP-0253317 850704

FDT IL--94754 A Div ex IL--75725; AU-644359 B Previous Publ. AU9054976; HU-208711 B Previous Publ. HU--38675, Based on WO8600639; DK-168709 B Previous Publ. DK8601028
PRAI 84US-0628342 840706; 84US-0652447 840919; 84US-0652742 840919; 84US-0628362 840706
AB WO 8600639 A UPAB: 930922
Recombinant colony stimulating factor (**CSF**) protein is claimed. It is prepd by isolating **CSF** protein as expressed from eukaryotic or prokaryotic host cells into which has been transformed a vector coding for the **CSF** protein.

Also claimed is a method for prepg and isolating a transformation vector contg. **CSF**/CDNa by (a) prepg. RNA from a cell that produces **CSF**, (b) prepg. polyadenylated mRNA from this, (c) prepg single stranded CDNA from mRNA, (d) converting the single stranded CDNA to double stranded cDNA, (e) inserting the double stranded cDNA into transformation vectors and transforming bacteria with the vector to form colonies (f) picking pools of 200-500 colonies and isolating plasmid DNA from each pool, (g) transfecting the plasmid DNA into suitable host cells for expressing **CSF** protein, (h) culturing the transfected cells and assaying the supernatant for **CSF** activity and selecting **CSF** positive pools and screening the colonies used to make the pool to identify a colony having **CSF** activity.

USE - The **CSF** proteins are growth and differentiation hormones for the cells of the myeloid system. They are used for treating infection or granulocytopenia or activating neutrophils in animals. The are e.g. indicated for use clinically for the treatment of myelo-suppression esp (symptomatic) granulocytopenia following chemotherapeutical or irradiation treatment of cancer. 0/7

L13 ANSWER 2 OF 16 WPIDS COPYRIGHT 1996 DERWENT INFORMATION LTD
AN 90-320231 [42] WPIDS
DNC C90-138655
TI Human macrophage migration inhibitory factor - used for treating cancer and infection enhancing wound healing and stimulating immune system.
DC B04 D16
IN **CLARK, S C**; WEISER, W
PA (BGHM) BRIGHAM & WOMENS HOSPITAL; (GEMY) GENETICS INST INC; (BRIG-N) BRIGHAM & WOMENS HOSPITA
CYC 15
PI WO9011301 A 901004 (9042)*
RW: AT BE CH DE DK ES FR GB IT LU NL SE
W: CA JP
EP-463037 A 920102 (9202)
R: AT BE CH DE ES FR GB IT LI LU NL SE
JP04504111 W 920723 (9236) 17 pp
ADT EP-463037 A 90EP-0904716 900315; JP04504111 W 90JP-0503914 900315, 90WO-US01355 900315
FDT JP04504111 W Based on WO9011301
PRAI 89US-0325408 890317
AB WO 9011301 A UPAB: 930928
A human macrophage migration inhibitory factor protein (MIF) free from association with other proteinaceous materials of formula (I) is new. Pref. the protein comprises all or a portion of the same

amino acid sequences or its fragments. DNA encoding the above sequence and transformed cells are also claimed. The MIF may also be administered with therapeutic amounts of a cytokine, haematoprotein, growth factor or tumour activated antibody. Specific cytokines are IL-1, IL-2, IL-3, IL-4, IL-6, GM-**CSF**, G-**CSF**, M-**CSF**, the interferons and erythropoietin.

USE/ADVANTAGE - Methods are claimed for treating cancer infection, enhancing wound healing and stimulating the immune system by administration to the patient of an effective amount of the factor. Generally, the daily dosage should be 1-1000 micrograms of the protein or 50-5000 units of protein per kg body weight. @ 0/0@

L13 ANSWER 3 OF 16 MEDLINE
AN 88016171 MEDLINE
TI Growth of human hemopoietic colonies in response to recombinant gibbon interleukin 3: comparison with human recombinant granulocyte and granulocyte-macrophage colony-stimulating factor.
AU Messner H A; Yamasaki K; Jamal N; Minden M M; Yang Y C; **Wong G G**; **Clark S C**
CS Ontario Cancer Institute, Toronto, Canada..
SO PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA, (1987 Oct) 84 (19) 6765-9.
Journal code: PV3. ISSN: 0027-8424.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
EM 8801
AB Supernatants of COS-1 cells transfected with gibbon cDNA encoding interleukin 3 (IL-3) with homology to sequences for human IL-3 were tested for ability to promote growth of various human hemopoietic progenitors. The effect of these supernatants as a source of recombinant IL-3 was compared to that of recombinant human granulocyte-macrophage colony-stimulating factor (GM-**CSF**) and granulocyte colony-stimulating factor (G-**CSF**) as well as to that of medium conditioned by phytohemagglutinin-stimulated leukocytes. The frequency of multilineage colonies, erythroid bursts, and megakaryocyte colonies in cultures containing the COS-1 cell supernatant was equivalent to the frequency observed in the controls and significantly higher than found in cultures plated with recombinant GM-**CSF**. **G-CSF** did not support the formation of multilineage colonies, erythroid bursts, and megakaryocyte colonies. In contrast, growth of granulocyte-macrophage colonies was best supported with GM-**CSF**, while recombinant IL-3 yielded colonies at lower or at best equivalent frequency. The simultaneous addition of higher concentrations of GM-**CSF** to cultures containing IL-3 in optimal amounts did not enhance the formation of multilineage colonies, erythroid bursts, and megakaryocyte colonies. However, the frequency of such colonies and bursts increased with GM-**CSF** when cultures were plated with suboptimal concentrations of IL-3. Growth of colonies within the granulocyte-macrophage lineage is optimally supported by GM-**CSF** and does not increase with further addition of IL-3.

L13 ANSWER 4 OF 16 MEDLINE

AN 87308821 MEDLINE
TI Stimulation of human hematopoietic colony formation by recombinant gibbon multi-colony-stimulating factor or interleukin 3.
AU Sieff C A; Niemeyer C M; Nathan D G; Ekern S C; Bieber F R; Yang Y C; **Wong G**; **Clark S C**
SO JOURNAL OF CLINICAL INVESTIGATION, (1987 Sep) 80 (3) 818-23.
Journal code: HS7. ISSN: 0021-9738.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Abridged Index Medicus Journals; Priority Journals; Cancer Journals
EM 8712
AB Recently, the gene for a novel mammalian hematopoietic growth factor homologous to murine interleukin 3 was isolated from a gibbon T cell line and expressed in monkey COS cells. The factor, termed multi-colony stimulating factor (multi-**CSF**) or interleukin 3, is stimulatory to human target cells. We investigated the range of enriched human bone marrow and fetal liver hematopoietic progenitors responsive to multi-**CSF**; compared the colony types observed with those obtained in the presence of recombinant granulocyte-macrophage **CSF** (GM-**CSF**); and analyzed the effects on colony formation of combining multi-**CSF** with GM-**CSF** or granulocyte-**CSF** (G-**CSF**). The results show that multi-**CSF** acts as a multipoietin. Alone it stimulates the formation of colonies derived from granulocyte, macrophage, eosinophil, and megakaryocyte progenitors. In combination with erythropoietin it supports the development of both erythroid and mixed colonies. Furthermore, the data show that multi-**CSF** is a more potent stimulus of erythroid progenitors than GM-**CSF**. In combination with G-**CSF** multi-**CSF** substantially increases granulocyte colony number over the number obtained with each factor alone. We conclude that multi-**CSF** may prove to have important therapeutic potential in vivo as a stimulus for hematopoiesis.

L13 ANSWER 5 OF 16 MEDLINE
AN 87300131 MEDLINE
TI The effects of three recombinant growth factors, IL-3, GM-**CSF**, and G-**CSF**, on the blast cells of acute myeloblastic leukemia maintained in short-term suspension culture.
AU Miyauchi J; Kelleher C A; Yang Y C; **Wong G G**; **Clark S C**; Minden M D; Minkin S; McCulloch E A
SO BLOOD, (1987 Sep) 70 (3) 657-63.
Journal code: A8G. ISSN: 0006-4971.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Abridged Index Medicus Journals; Priority Journals; Cancer Journals
EM 8712
AB The blast stem cells of acute myeloblastic leukemia (AML) respond in cell culture to growth factors by both self-renewal and terminal divisions. Both of these functions have been shown to be stimulated by the recombinant growth factors granulocyte-macrophage colony-stimulating factor (GM-**CSF**) and granulocyte colony-stimulating factor (G-**CSF**). In this paper, recombinant gibbon interleukin-3 (IL-3), homologous to human IL-3,

was tested on blast cells and compared with the effects of GM-**CSF**, G-**CSF**, and medium conditioned by the bladder cell line 5637 (5637-CM). We found that IL-3 was an effective stimulator of blast renewal and terminal divisions. However, great patient-to-patient variation was found. A graphic method of presenting complex comparisons between growth factors is also included.

L13 ANSWER 6 OF 16 MEDLINE
AN 89062731 MEDLINE
TI Growth regulation of human acute myeloid leukemia: effects of five recombinant hematopoietic factors in a serum-free culture system.
AU Delwel R; Salem M; Pellens C; Dorssers L; Wagemaker G; **Clark S**; Lowenberg B
CS Dr Daniel den Hoed Cancer Center, Rotterdam, The Netherlands..
SO BLOOD, (1988 Dec) 72 (6) 1944-9.
Journal code: A8G. ISSN: 0006-4971.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Abridged Index Medicus Journals; Priority Journals; Cancer Journals
EM 8903
AB The response of human acute myeloid leukemia (AML) cells to the distinct hematopoietic growth factors (HGFs), ie, recombinant interleukin-3 (IL-3), granulocyte-macrophage-**CSF** (GM-**CSF**), granulocyte-**CSF** (**G-CSF**), macrophage-**CSF** (M-**CSF**), and erythropoietin (Epo) was investigated under well-defined serum-free conditions. Proliferative responses to these factors, when added separately as well as in combinations, were analyzed in 25 cases of human AML using 3H-thymidine incorporation and colony assays. The 3H-thymidine uptake data revealed that IL-3, GM-**CSF**, G-**CSF**, and M-**CSF** were stimulators of AML proliferation in 19, 15, 13, and 4 cases, respectively. Epo only stimulated DNA synthesis in the cells of the single erythroleukemia case. GM-**CSF** stimulation was seen only in IL-3 reactive cases and GM-**CSF**, when combined with IL-3, could not further elevate the DNA synthesis evoked by IL-3 alone. On the other hand, in six cases, G-**CSF** enhanced the IL-3- or GM-**CSF**-stimulated thymidine uptake. These results suggest that subpopulations of AML cells that are activated by distinct CSFs (eg, IL-3/GM-**CSF**-responsive cells and G-**CSF**-responsive cells) coexist. The 3H-thymidine incorporation assay was more sensitive for measuring **CSF** responses than methylcellulose colony cultures, since activation of DNA synthesis was more frequently seen than induction of colony formation. DNA synthesis experiments revealed eight different **CSF** response patterns among these 25 cases. **CSF** phenotyping may be a useful addition to the morphologic classification of AML, since these patterns directly reflect the ability of the proliferating subsets of AML cells to respond to the CSFs.

L13 ANSWER 7 OF 16 MEDLINE
AN 88231775 MEDLINE
TI The effects of combinations of the recombinant growth factors GM-**CSF**, G-**CSF**, IL-3, and **CSF**-1 on leukemic blast cells in suspension culture.

AU Miyauchi J; Kelleher C A; **Wong G G**; Yang Y C; **Clark S C**; Minkin S; Minden M D; McCulloch E A
CS The Ontario Cancer Institute, Toronto, Canada..
SO LEUKEMIA, (1988 Jun) 2 (6) 382-7.
Journal code: LEU. ISSN: 0887-6924.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
EM 8809
AB The blast cells of acute myeloblastic leukemia may be considered as a renewal population maintained by stem cells that are capable of both self-renewal and differentiation. Blast stem cells grow in culture usually when stimulated by growth factors normally active on myelopoietic cells. Two culture methods permit an evaluation of the balance between self-renewal and differentiation; previous studies have shown that this balance can be affected by recombinant growth factors. These include interleukin 3 (IL-3) and granulocyte-macrophage colony stimulating factor (GM-**CSF**), active on early cells in normal myelopoiesis, and G-**CSF** and **CSF**-1, restricted in normal hemopoiesis to the granulopoietic and macrophage/monocytic lineages, respectively. In this paper we report the results of evaluating the effects on these recombinant growth factors alone or in mixtures of two at optimal concentrations. The results were obtained either using titrations of colony formation in methylcellulose or growth in suspension. Star diagrams, a technique from exploratory data analysis, were used to provide quantitative and graphic displays of the results of the recombinant factors on the balance between blast self-renewal and differentiation. Blasts from 4 acute myeloblastic leukemia patients and one patient with the blast crisis of chronic myeloblastic leukemia were examined in detail. The great patient-to-patient variation usually observed was seen in both plating efficiency in methylcellulose and growth pattern in suspension. In spite of this variation, a common pattern of response to growth factors emerged. When the early acting factors, IL-3 and GM-**CSF**, were combined, the effect was quantitatively and qualitatively similar to the largest stimulation seen with either of the factors alone. In contrast, late-acting factors, G-**CSF** and **CSF**-1, influenced each other's effects when present together and each affected the activities of GM-**CSF** and IL-3. Notably, **CSF**-1, which often led to the accumulation of adherent, terminal cells in suspension, usually maintained or increased this differentiation-like activity in combination. G-**CSF** also favored differentiation in combination, although the effect was usually to increase the number of colonies in methylcellulose, most of which consist of blast cells incapable of further divisions. The results are discussed as they relate to the postulated structure of the blast population and the normal targets of the recombinant growth factors.

L13 ANSWER 8 OF 16 MEDLINE
AN 88222393 MEDLINE
TI Recombinant gibbon interleukin-3 acts synergistically with recombinant human G-**CSF** and GM-**CSF** in vitro.
AU Paquette R L; Zhou J Y; Yang Y C; **Clark S C**; Koeffler H P
CS Department of Medicine, UCLA Medical Center..

NC CA 26038
CA 32737
CA 33936
+
SO BLOOD, (1988 Jun) 71 (6) 1596-600.
Journal code: A8G. ISSN: 0006-4971.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Abridged Index Medicus Journals; Priority Journals; Cancer Journals
EM 8809
AB Recombinant gibbon interleukin-3 (IL-3) is a multilineage hematopoietic colony-stimulating factor (**CSF**) that recently was cloned and found to be highly homologous with human IL-3. Gibbon IL-3, as well as human granulocyte-**CSF** (**G-CSF**) and human granulocyte-macrophage **CSF** (GM-**CSF**), stimulated normal human bone marrow cells to form myeloid colonies in soft agar in a sigmoidal dose-response manner. When IL-3 was added to increasing concentrations of G-**CSF** or GM-**CSF**, synergistic colony formation occurred as compared with the effects of each **CSF** alone. Synergism was also noted when G-**CSF** was added with GM-**CSF** and when all the CSFs were added simultaneously. The combination of IL-3 and GM-**CSF** was less stimulatory than all the other **CSF** combinations. At day 11 of culture, IL-3 induced granulocyte-macrophage (38%), eosinophil (30%), granulocyte (18%), and macrophage (14%) colony formation. In summary, gibbon IL-3 is a growth factor that can synergize with other CSFs to enhance proliferation of myeloid-committed progenitors, suggesting that combinations of CSFs may have clinical utility in patients with neutropenia of various etiologies.

L13 ANSWER 9 OF 16 MEDLINE
AN 88213448 MEDLINE
TI The effects of recombinant **CSF**-1 on the blast cells of acute myeloblastic leukemia in suspension culture.
AU Miyauchi J; Wang C; Kelleher C A; **Wong G G**; **Clark S C**; Minden M D; McCulloch E A
CS Ontario Cancer Institute, Toronto, Canada..
SO JOURNAL OF CELLULAR PHYSIOLOGY, (1988 Apr) 135 (1) 55-62.
Journal code: HNB. ISSN: 0021-9541.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
EM 8808
AB Recombinant hemopoietic colony-stimulating factors (CSFs), including GM-**CSF**, **G-CSF** and IL-3, have been shown to be effective stimulators of both self-renewal and terminal differentiation of blast stem cells in acute myeloblastic leukemia (AML). We have examined the activity of a fourth growth factor, recombinant **CSF**-1 (or M-**CSF**), on the growth of leukemic blasts in culture. **CSF**-1 was found to be active on some, but not all, blast populations. In sensitive cells, **CSF**-1 often stimulated the production of adherent blast cells incapable of division. This observation leads us to suggest

that **CSF**-1 may be useful in the treatment of selected cases of AML.

L13 ANSWER 10 OF 16 MEDLINE
AN 88153947 MEDLINE
TI Interleukin-1 regulation of hematopoietic growth factor production by human stromal fibroblasts.
AU Yang Y C; Tsai S; **Wong G G**; **Clark S C**
CS Genetics Institute, Cambridge, Massachusetts 02140..
SO JOURNAL OF CELLULAR PHYSIOLOGY, (1988 Feb) 134 (2) 292-6.
Journal code: HNB. ISSN: 0021-9541.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
EM 8806
AB The human stromal fibroblastoid cell strain designated ST-1 represents a normal population of cells capable of supporting hematopoiesis in vitro. These cells constitutively elaborate hematopoietic growth factor activity into the medium and the level of production of this activity dramatically increases following stimulation of the cells with IL-1. This enhanced production is due at least in part to increased expression of the genes for GM-**CSF**, G-**CSF**, and IL-6, but not IL-3. The IL-1 treatment had little effect on the expression of M-**CSF**, a factor made constitutively by the cells. These results are consistent with the model that hematopoiesis is regulated at least in part by constant short-range interactions of humoral factors produced by stromal cells both with other types of stromal cells and with the hematopoietic progenitors.

L13 ANSWER 11 OF 16 HCAPLUS COPYRIGHT 1996 ACS
AN 1988:547668 HCAPLUS
DN 109:147668
TI Recombinant human monocyte specific colony-stimulating factor stimulates both immature and mature cells of human monocyte lineage
AU Motoyoshi, K.; Yoshida, K.; Hatake, K.; Yanai, N; Kawashima, T.; Saito, M.; Miura, Y.; **Wong, G. G.**; Fujisawa, M.; et al.
CS Jichi Med. Sch., Tochigi, 329-04, Japan
SO Prog. Leukocyte Biol. (1988), 8(Monokines Other Non-Lymphocytic Cytokines), 301-6
CODEN: PLBIE5; ISSN: 0884-6790
DT Journal
LA English
AB Purified human monocyte-specific colony-stimulating factor (hM-**CSF**) stimulated adherent cell-depleted bone marrow cells to form macrophagic colonies. In culture human monocytes mainly produce granulocyte-**CSF** (**G-CSF**) in the absence of hM-**CSF** and produce both hG-**CSF** and human granulocyte/macrophage-**CSF** in the presence of hM-**CSF**.

L13 ANSWER 12 OF 16 MEDLINE
AN 90216467 MEDLINE
TI Interleukin-3: molecular biology and biologic activities.
AU Yang Y C; **Clark S C**
CS Genetics Institute, Inc., Cambridge, Massachusetts..

SO HEMATOLOGY/ONCOLOGY CLINICS OF NORTH AMERICA, (1989 Sep) 3 (3) 441-52. Ref: 63
Journal code: HEO. ISSN: 0889-8588.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW LITERATURE)
LA English
FS Priority Journals
EM 9007
AB IL-3 is one of the primary factors capable of supporting the growth and development of hematopoietic cells in culture. In comparison with the other hematopoietic growth factors, IL-3 preferentially supports the proliferation of early multilineage progenitors or progenitors at early stages of development within the different lineages. Subsequently, the developing cells lose responsiveness to IL-3 while acquiring dependence on the later acting factors: GM-**CSF**, G-**CSF**, M-**CSF**, or Ep. In addition, IL-3 has been demonstrated to exert biologic effects with other target cell populations. These activities include the potentiation of the IL-2-dependent growth of normal T cells; the potentiation of the IL-2-dependent secretion of IgG by activated B cells; and the potentiation of the activities of eosinophils, basophils, and monocytes. The importance of any of these activities of IL-3 in vivo in either normal or stressed animals remains to be determined. Initial experiments in primates with IL-3 have yielded results consistent with its role as a regulator of early hematopoietic cell development. Although administration of IL-3 alone has relatively little effect on the levels of circulating blood cells, this treatment primes the animals to become hyper-responsive to subsequent administration of the later acting factors GM-**CSF** and Ep. Thus combinations of factors, at least in some situations, can provide a more potent stimulation of hematopoiesis than provided by the individual molecules, a finding that should greatly expand the utility of the different hematopoietins to more indications in the clinic.

L13 ANSWER 13 OF 16 MEDLINE
AN 90028776 MEDLINE
TI Granulocyte-macrophage colony-stimulating factor is an endogenous regulator of cell proliferation in juvenile chronic myelogenous leukemia.
AU Gualtieri R J; Emanuel P D; Zuckerman K S; Martin G; **Clark S C**; Shadduck R K; Dracker R A; Akabutu J; Nitschke R; Hetherington M L; et al
CS Department of Medicine, Children's Hospital of Alabama, Birmingham..
NC CA 15237
CA 25408
DK07488
SO BLOOD, (1989 Nov 15) 74 (7) 2360-7.
Journal code: A8G. ISSN: 0006-4971.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Abridged Index Medicus Journals; Priority Journals; Cancer Journals
EM 9002
AB Juvenile chronic myelogenous leukemia (JCML) is a rare

myeloproliferative disorder of early childhood that is clinically and cytogenically distinct from the well-recognized adult type of chronic myeloid leukemia. Unlike the adult disease, growth of hematopoietic progenitors from peripheral blood (PB) occurs in the absence of exogenous stimulus even at low cell densities. This so-called "spontaneous" growth can be abrogated by adherent cell depletion and appears to depend on production of endogenous growth factors. We studied seven children with JCML to determine the nature of endogenous stimulators. With isolated PB mononuclear cells (PBMNCs) and a 3H-thymidine (3H-TdR) incorporation assay, JCML cells were shown to incorporate high levels of 3H-TdR when cultured in the absence of stimulus even at low cell densities. When neutralizing antisera prepared against each of the four known colony-stimulating factors (CSFs), GM-**CSF**, **G-CSF**, M-**CSF**, and interleukin-3 (IL-3), as well as antisera against interleukin-1 (alpha and beta) and tumor necrosis factor (TNF) were added to these cultures, only the antisera against recombinant human GM-**CSF** (rhGM-**CSF**) consistently resulted in significant inhibition of cell proliferation, achieving up to 72% inhibition of 3H-TdR incorporation in one case. Monoclonal antibodies (MoAbs) against rhGM-**CSF** resulted in a similar and highly significant degree of inhibition. A marked inhibitory effect of rhGM-**CSF** antiserum on "spontaneous" growth of PB CFU-GM derived colonies in semisolid medium was also demonstrated in four of five patients studied (87% to 90% inhibition). Production of growth factors by highly enriched JCML monocytes was variable. When initially studied in five of the seven patients, the monocytes from three of the patients revealed increased release of IL-1-like activities; two patients had levels similar to those of controls. One patient with normal levels when initially studied was later shown to have markedly increased amounts of IL-1-like activities in a second preparation of monocyte-conditioned medium (MCM). High levels of GM-**CSF** were detected in the initial MCM from one patient, but this may have indirectly reflected elevated IL-1-like activities present in the MCM. IL-3 and M-**CSF** levels were either low or undetectable in the patients studied as compared with MCM prepared with normal adult monocytes. These results clearly implicate GM-**CSF** as the primary endogenous regulator of JCML cell proliferation in culture and suggest that this malignant myeloproliferative disease may in part result from paracrine stimulation of marrow progenitor cells by growth factors/cytokines secreted by the malignant monocytes.

L13 ANSWER 14 OF 16 MEDLINE
AN 89323323 MEDLINE
TI Action of interleukin-3, G-**CSF**, and GM-**CSF** on highly enriched human hematopoietic progenitor cells: synergistic interaction of GM-**CSF** plus G-**CSF**.
AU McNiece I; Andrews R; Stewart M; **Clark S**; Boone T; Quesenberry P
CS Department of Internal Medicine, University of Virginia, Charlottesville..
NC RO1AM27424
RO1CA27466
RO1DK33298
SO BLOOD, (1989 Jul) 74 (1) 110-4.
Journal code: A8G. ISSN: 0006-4971.

CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Abridged Index Medicus Journals; Priority Journals; Cancer Journals
EM 8911
AB Purified preparations of recombinant human granulocyte-macrophage colony-stimulating factor (GM-**CSF**), granulocyte **CSF** (G-**CSF**), and interleukin 3 (IL-3 or multi-**CSF**) alone and in combination, have been compared for their stimulatory effects on human granulocyte-macrophage colony forming cells (GM-CFC). In cultures of unseparated normal human bone marrow, the combinations of G-**CSF** plus IL-3 and GM-**CSF** plus IL-3 stimulated additive numbers of GM colonies, while GM-**CSF** plus G-**CSF** stimulated greater than additive numbers of GM colonies, compared with the sum of the colony formation obtained with each factor alone. Cultures of unseparated bone marrow, harvested from patients four to six days after administration of 5-fluorouracil (5-FU), resulted in additive GM colony formation with GM-**CSF** plus G-**CSF**, GM-**CSF** plus IL-3, and G-**CSF** plus IL-3. In order to address the possibility of secondary factor involvement in the synergistic interaction of GM-**CSF** and G-**CSF**, CD33+/CD34+ colony forming cells were separated from normal and post FU marrow by two color fluorescence activated cell sorting. In cultures of CD33+/CD34+ cells the combination of GM-**CSF** plus G-**CSF** stimulated a synergistic increase in GM colonies while GM-**CSF** plus IL-3 stimulated additive numbers of colonies. These results suggest that GM-**CSF**, **G-CSF**, and IL-3 stimulate distinct populations of GM-CFC. Furthermore GM-**CSF** and G-**CSF** interact synergistically and this action is a direct effect on progenitor cells not stimulated by GM-**CSF** or G-**CSF** alone.

L13 ANSWER 15 OF 16 MEDLINE
AN 89194115 MEDLINE
TI Maturation of human acute myeloid leukaemia in vitro: the response to five recombinant haematopoietic factors in a serum-free system.
AU Salem M; Delwel R; Mahmoud L A; **Clark S**; Elbasousy E M; Lowenberg B
CS Dr Daniel den Hoed Cancer Center, Rotterdam, The Netherlands..
SO BRITISH JOURNAL OF HAEMATOLOGY, (1989 Mar) 71 (3) 363-70. Journal code: AXC. ISSN: 0007-1048.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
EM 8907
AB The abilities of human recombinant IL-3, GM-**CSF**, **G-CSF**, M-**CSF** and Epo to induce maturation in human AML cells in vitro were investigated using cell specimens from 25 AML patients. The experiments were carried out under exactly defined serum-free culture conditions. In the absence of CSFs, monocytic and/or granulocytic maturation was detected in 14/25 cases. IL-3, GM-**CSF**, **G-CSF** and M-**CSF** elevated the proportions of monocyte/macrophages in 3/25, 2/25, 1/25 and 6/25 cases respectively, and increased the percentages of mature granulocytes in 2/25, 1/25, 1/25 and 0/25

cases, and if so only to a limited extent (values below 50%). The 3H-thymidine (3H-TdR) uptake studies revealed that IL-3, GM-**CSF**, G-**CSF** and M-**CSF** were efficient stimulators of DNA synthesis of AML cells in 19, 15, 13 and four of those cases, respectively. Thus, although the cells in most cases responded to CSFs by activation of DNA synthesis, they were unable to give rise to terminally differentiated stages. Provision of CSFs in combination was more frequently effective in enhancing maturation and also increased the magnitude of maturation response. Monocytic versus granulocytic maturation of AML cells after culture did not correlate with the FAB cytology nor with the type of **CSF** presented; but generally granulocytic maturation was an infrequent phenomenon. Epo stimulated erythroid differentiation and DNA synthesis only in the case of erythroleukaemia, but it had no effect on the cells of 10 other AML cases. Extrapolation of these in vitro findings would suggest that CSFs would have a limited therapeutic utility to induce AML cell maturation in vivo and that hazards of stimulating blast cell proliferation with these factors may be anticipated.

L13 ANSWER 16 OF 16 MEDLINE
AN 91114747 MEDLINE
TI Multifactor stimulation of megakaryocytopoiesis: effects of interleukin 6.
AU Quesenberry P J; McGrath H E; Williams M E; Robinson B E; Deacon D H; **Clark S**; Urdal D; McNiece I K
CS University of Virginia Health Sciences Center, Department of Internal Medicine, School of Medicine, Charlottesville 22908..
NC RO1-AM27424 (NIADDK)
RO1-AI23869 (NIAID)
RO1-AM27466 (NIADDK)
+
SO EXPERIMENTAL HEMATOLOGY, (1991 Jan) 19 (1) 35-41.
Journal code: EPR. ISSN: 0301-472X.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
EM 9105
AB We have previously demonstrated that interleukin 3 (IL-3), granulocyte-macrophage colony-stimulating factor (GM-**CSF**), and granulocyte colony-stimulating factor (G-**CSF**) stimulate various aspects of megakaryocytopoiesis. We have investigated the capacity of interleukin 6 (IL-6) to stimulate megakaryocyte colony formation from both normal Balb/C marrow and light-density marrow extensively depleted of adherent, pre-B, B and T cells. Human recombinant IL-6 (167 ng/ml) stimulated megakaryocyte colony formation from normal marrow (8.6 +/- 1 megakaryocyte colony-forming units [CFU-meg]/10(5) cells) as compared to control (1.5 +/- 4 CFU-meg/10(5) cells) in 16 determinations (p less than 0.01). IL-6 (167 ng/ml) also stimulated CFU-meg formation from depleted marrow (control, 10.8 +/- 4 CFU-meg/10(5) cells versus IL-6, 68 +/- 19 CFU-meg/10(5) cells in 12 determinations, p less than 0.01). IL-6 synergistically augmented IL-3-induced colony formation (139% IL-3 control, 120% calculated IL-3 plus IL-6 control, n = 11, p less than 0.01) in normal marrow and showed an additive effect in depleted marrow (133% IL-3 control, p less than

0.01, 114% of IL-3 plus IL-6, value not significant [NS] at 0.05 level). Studies with recombinant murine IL-6 gave similar results. There was an increasing level of megakaryocyte colony-stimulating activity from G-**CSF** (16,667 U/ml, 2.47 +/- 0.6 CFU-meg/10(5) cells, n = 17), to IL-6 (167 ng/ml, 8.47 +/- 0.96 CFU-meg/10(5) cells, n = 19), to GM-**CSF** (52 U/ml, 23 +/- 4 CFU-meg/10(5) cells, n = 14), to IL-3 (167 U/ml, 48 +/- 5 CFU-meg/10(5) cells, n = 20) as compared to media-stimulated marrow (range 1.29-1.86 CFU-meg/10(5) cells). A similar hierarchy was seen with depleted marrow. Combinations of factors (including IL-3, GM-**CSF**, G-**CSF**, and IL-6) tested against normal unseparated murine marrow did not further augment CFU-meg numbers over IL-3 plus IL-6 but did increase colony size. These data suggest that IL-6 is an important megakaryocyte regulator, that at least four growth factors interact synergistically or additively to regulate megakaryocytopoiesis, and that combinations of growth factors, possibly in physical association, might be critical in stimulating megakaryocyte stem cells.

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=> file hom;d his
FILE 'HOME' ENTERED AT 16:29:30 ON 22 JUN 96


     (FILE 'HOME' ENTERED AT 16:19:19 ON 22 JUN 96)

     INDEX 'MEDLINE, HCAPLUS, EMBASE, BIOSIS, WPIDS, IFIPAT, BIOTECHDS,
     DISSABS, CONFSCI, LIFESCI, SCISEARCH, JAPIO, JICST-EPLUS' ENTERED
     AT 16:19:40 ON 22 JUN 96
                SEA (CLARK,S? OR CLARK, S? OR CLARK S? OR KAUFMAN,R? OR K
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            3031   FILE HCAPLUS
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            3461*  FILE BIOSIS
             292   FILE WPIDS
             338   FILE IFIPAT
             109   FILE BIOTECHDS
             245*  FILE DISSABS
             442*  FILE CONFSCI
             687*  FILE LIFESCI
            4399*  FILE SCISEARCH
              37   FILE JICST-EPLUS
L1              QUE (CLARK,S? OR CLARK, S? OR CLARK S? OR KAUFMAN,R? OR K
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                SEA L1 AND CSF
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             115*  FILE EMBASE
             146*  FILE BIOSIS
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               1*  FILE CONFSCI
              65*  FILE LIFESCI
              97*  FILE SCISEARCH
L2              QUE L1 AND CSF
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                SEA L2 AND (CSF ILE# OR CSF THR OR CSF G)
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               0*  FILE DISSABS
               0*  FILE CONFSCI
               6*  FILE LIFESCI
               2*  FILE SCISEARCH
L3              QUE L2 AND (CSF ILE# OR CSF THR OR CSF G)
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     FILE 'MEDLINE, EMBASE, BIOSIS, HCAPLUS, LIFESCI, WPIDS, SCISEARCH'
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; ID P60535 standard; Protein; 144 AA.
; AC P60535;
; DT 30-JUL-1991 (first entry)
; DE Colony stimulating factor (CSF) variant.
; KW Colony stimulating factor.
; OS Homo sapiens.
; FH Key Location/Qualifiers
; FT Misc_difference 20 Xaa
; FT /label= Ser in gibbon CSF
; FT Misc_difference 27 Xaa
; FT /label= Arg in gibbon CSF
; FT Misc_difference 58
; FT /label= Ile in gibbon CSF
; FT Misc_difference 60
; FT /label= Val in gibbon CSF
; FT Misc_difference 117
; FT /label= Thr in human CSF-Thr
; FT Misc_difference 117
; FT /label= Ile in human CSF-Ile
; FT Misc_difference 134
; FT /label= Thr in gibbon CSF
; FT Misc_difference 143
; FT /label= Gly in gibbon CSF
; PN WO8600639-A.
; PD 30-JAN-1986.
; PF 04-JUL-1985; E00326.
; PR 06-JUL-1984; US-628342.
; PR 19-SEP-1984; US-652742.
; PR 19-SEP-1984; US-652447.
; PA (SANO) SANDOZ AG.
; PI Clark SC, Kaufman RJ, Wong GG, Wang EA.
; DR WPI; 86-042122/06.
; DR N-PSDB; N60457.
; PT Recombinant colony stimulating factor protein - used for treating
; PT infection or granulocytopenia or activating neutrophils in
; PT animals.
; PS Disclosure; Fig 1; 91pp; English.
; CC The sequence are human CSF variants (CSF-Ile and CSF-Thr), and
; CC gibbon granulocyte-macrophage CSF. The CSFs are lymphokines used
; CC to treat myelosuppression, especially sympotamatic
; CC granulocytopaenia.
; SQ Sequence 144 AA;
; SQ 9 A; 5 R; 4 N; 4 D; 0 B; 5 C; 10 Q; 13 E; 0 Z; 4 G; 3 H;
; SQ 5 I; 19 L; 6 K; 5 M; 5 F; 11 P; 12 S; 13 T; 3 W; 2 Y; 6 V;
; CC Retrieved by shah on Fri 21 Jun 96 11:53:45-PDT using FindSeq
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pvqel

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*********************************
*      WELCOME TO THE           *
*   U.S. PATENT TEXT FILE       *
*********************************

=> s (GM-CSF or granulocyte macrophage colony stimulating factor)

     43316 GM
      4175 CSF
      1228 GM-CSF
           (GM(W)CSF)
      1785 GRANULOCYTE
      3696 MACROPHAGE
     11839 COLONY
     19949 STIMULATING
    254482 FACTOR
       581 GRANULOCYTE MACROPHAGE COLONY STIMULATING FACTOR
           (GRANULOCYTE(W)MACROPHAGE(W)COLONY(W)STIMULATING(W)FACTOR
)
L1      1347 (GM-CSF OR GRANULOCYTE MACROPHAGE COLONY
STIMULATING FACTOR
)

=> s l1 (5a) (protein? or polypeptide?)

     80354 PROTEIN?
     18627 POLYPEPTIDE?
L2      136 L1 (5A) (PROTEIN? OR POLYPEPTIDE?)

=> s l1 (p) (recombinant?)

     17205 RECOMBINANT?
L3      379 L1 (P) (RECOMBINANT?)

=> d l2 1-36 cit
```

1. 5,783,583, Jul. 21, 1998, 17-(cyclopropylmethyl)-4,5alpha-epoxy-6-methylenemorphinan-3,14-diol, hydrochloride salt for the purpose of rapid narcotic detoxification; David Lew Simon, 514/282, 281; 546/45 [IMAGE AVAILABLE]

2. 5,814,517, Sep. 29, 1998, DNA spacer regulatory elements responsive to cytokines and methods for their use; H. Martin Seidel, et al., 435/325, 69.1, 320.1; 536/23.1, 23.2, 23.5, 24.1 [IMAGE AVAILABLE]

3. 5,814,482, Sep. 29, 1998, Eukaryotic layered vector initiation systems; Thomas W. Dubensky, Jr., et al., 435/69.3, 320.1; 536/23.1, 24.1 [IMAGE AVAILABLE]

4. 5,811,300, Sep. 22, 1998, TNF-.alpha. ribozymes; Sean Sullivan, et al., 435/366, 6, 91 31, 320.1, 325; 514/44; 536/23.1, 23.2, 24.5 [IMAGE AVAILABLE]

5. 5,811,231, Sep. 22, 1998, Methods and kits for eukaryotic gene profiling; Spencer B. Farr, et al., 435/6; 424/94.1, 178.1, 278.1, 600; 435/29, 32, 91.2, 870; 536/23.1, 24.1, 24 3, 24.33 [IMAGE AVAILABLE]

6. 5,808,008, Sep. 15, 1998, Method of producing human pluripotent hematopoietic colony stimulating factor; Karl Welte, et al., 530/412; 435/69.5; 530/416, 417, 418, 420 [IMAGE AVAILABLE]

7. 5,807,743, Sep. 15, 1998, Interleukin-2 receptor gamma-chain ribozymes; Dan T. Stinchcomb, et al., 435/366, 6, 91.31, 320.1, 325; 536/23.1, 23.2, 24.5 [IMAGE AVAILABLE]

8. 5,807,698, Sep. 15, 1998, Human cyclin E; James M. Roberts, et al., 435/69.1, 6, 320.1, 326; 536/23.5, 24.31, 24.33 [IMAGE AVAILABLE]

9. 5,795,966, Aug. 18, 1998, Antagonists of interleukin-15; Kenneth H. Grabstein, et al., 530/388.23; 424/158.1; 435/326, 328, 335, 346, 352 [IMAGE AVAILABLE]

10. 5,789,247, Aug. 4, 1998, Expression in non-tumoral human lymphoblastoid lines with an integrative vector; Annick Ballay, et al., 435/372.2, 69.1, 320.1; 536/23.1, 24.1 [IMAGE AVAILABLE]

11. 5,789,245, Aug. 4, 1998, Alphavirus structural protein expression cassettes; Thomas W. Dubensky, Jr., et al., 435/320.1, 69.1, 325; 536/23.72 [IMAGE AVAILABLE]

12. 5,789,192, Aug. 4, 1998, Mammalian receptors for interleukin-10 (IL-10); Kevin W. Moore, et al., 435/69.1, 252.3, 320.1; 536/23.5, 24.3 [IMAGE AVAILABLE]

13. 5,783,661, Jul. 21, 1998, Human cyclin E polypeptides; James M. Roberts, et al., 530/300, 350; 536/23.5 [IMAGE AVAILABLE]

14. 5,777,193, Jul. 7, 1998, Animals with targeted gene disruption; Ashley Roger Dunn, et al., 800/3; 424/9.1, 9.2; 435/4; 800/9, 11, 18 [IMAGE AVAILABLE]

15. 5,773,246, Jun. 30, 1998, Methods and compositions useful in the recognition, binding and expression of ribonucleic acids involved in cell growth, neoplasia and immunoregulation; Jack D. Keene, et al., 435/69.1, 488, 489; 530/350; 536/23.1 [IMAGE AVAILABLE]

16. 5,772,992, Jun. 30, 1998, Compositions for co-administration of interleukin-3 mutants and other cytokines and hematopoietic factors; S. Christopher Bauer, et al., 424/85.2, 85.1; 435/69.52 [IMAGE AVAILABLE]

17. 5,762,921, Jun. 9, 1998, Composition and methods for the treatment of tumors; Gordon A. Vehar, 424/85.1, 85.2, 85.5, 158.1, 198.1; 514/12; 530/350, 351, 381 [IMAGE AVAILABLE]

18. 5,747,471, May 5, 1998, Cationic amphiphiles containing steroid lipophilic groups for intracellular delivery of therapeutic molecules; Craig S. Siegel, et al., 514/44, 182, 777; 552/544; 560/6 [IMAGE AVAILABLE]

19. 5,744,361, Apr. 28, 1998, Expansion of human hematopoietic progenitor cells in a liquid medium; Ronald Hoffman, et al., 435/372; 424/93.7; 435/366, 383, 384, 385, 386, 404, 405, 406 [IMAGE AVAILABLE]

20. 5,739,118, Apr. 14, 1998, Compositions and methods for delivery of genetic material; Richard A. Carrano, et al., 514/44; 424/184.1, 278.1; 435/69.1, 69.3, 375; 514/25, 27, 33, 35, 54, 510, 680, 731, 732 [IMAGE AVAILABLE]

21. 5,738,849, Apr. 14, 1998, Interleukin-3 (IL-3) variant fusion proteins, their recombinant production, and therapeutic compositions comprising them; S. Christopher Bauer, et al., 424/192.1, 85.1, 85.2, 195.11; 435/69.5, 69.52, 69.7; 530/351; 536/23.4, 23.5, 23.52 [IMAGE AVAILABLE]

22. 5,736,524, Apr. 7, 1998, Polynucleotide tuberculosis vaccine; Jean Content, et al., 514/44; 435/6, 69.1, 320.1, 375 [IMAGE AVAILABLE]

23. 5,734,036, Mar. 31, 1998, Nucleic acids encoding transcriptional activators; Richard A. Maki, et al., 536/23.1; 435/320.1, 325; 536/24.5 [IMAGE AVAILABLE]

24. 5,730,970, Mar. 24, 1998, Pharmaceutical compositions comprising human interleukin-4 (IL-4); Frank Lee, et al., 424/85.2; 435/69.52, 71.1, 252.3, 254.2, 320.1, 325; 514/2, 8, 12 [IMAGE AVAILABLE]

25. 5,726,036, Mar. 10, 1998, Granulocyte-macrophage colony-stimulating factor receptor and derivatives thereof; Nicos Anthony Nicola, et al., 435/69.1, 252.3, 320.1; 536/23.5, 24.3 [IMAGE AVAILABLE]

26. 5,721,206, Feb. 24, 1998, Pharmaceutical composition for use as a retinal pigment epithelial cell growth agent; Takao Tobe, et al., 514/2, 885, 912 [IMAGE AVAILABLE]

27. 5,720,952, Feb. 24, 1998, Method of treating myelo-suppression with GM-CSF; Steven C. Clark, et al., 424/85.1, 184.1, 198.1; 514/2, 8, 12, 885 [IMAGE AVAILABLE]

28. 5,716,805, Feb. 10, 1998, Methods of preparing soluble, oligomeric proteins; Subhashini Srinivasan, et al., 435/69.1, 7.2, 69.7, 70.1, 71.1, 252.3, 320.1, 325; 530/350; 536/23.1, 23.5 [IMAGE AVAILABLE]

29. 5,714,316, Feb. 3, 1998, Chimeric envelope proteins for viral targeting; David Weiner, et al., 435/6, 5, 69.1, 69.7, 320.1, 325, 348, 352, 357, 358, 364, 365, 367; 536/23.1, 23.4 [IMAGE AVAILABLE]

30. 5,712,094, Jan. 27, 1998, Methods for detecting modulators of cytokine action; H. Martin Seidel, et al., 435/6, 252.3, 320.1, 325; 536/23.1 [IMAGE AVAILABLE]

31. 5,707,803, Jan. 13, 1998, DNA regulatory elements responsive to cytokines and methods for their use; Ian Peter Lamb, et al., 435/6, 69.1, 320.1; 536/24.1 [IMAGE AVAILABLE]

32. 5,705,611, Jan. 6, 1998, Human GM-CSF receptor component; Kazuhiro Hayashida, et al., 530/350; 435/69.1; 536/23.5 [IMAGE AVAILABLE]

33. 5,705,151, Jan. 6, 1998, Gene therapy for T cell regulation; Steve W. Dow, et al., 424/93.21, 450; 435/7.2, 69.1, 320.1, 458; 514/44 [IMAGE AVAILABLE]

34. 5,702,919, Dec. 30, 1997, DNA encoding canine granulocyte macrophage colony stimulating factor; Richard A. Nash, et al., 435/69.5, 252.3, 254.2, 320.1, 360, 364, 365.1, 367; 536/23.5 [IMAGE AVAILABLE]

35. 5,698,446, Dec. 16, 1997, Methods and compositions for inhibiting production of replication competent virus; Wolfgang M. Klump, et al., 435/350, 320.1, 366 [IMAGE AVAILABLE]

36. 5,698,427, Dec. 16, 1997, Methods and compositions involved in cell growth, neoplasia and immunoregulation; Jack D. Keene, et al., 435/456, 458; 530/350 [IMAGE AVAILABLE]

=> d l2 37-136 cit

37. 5,696,086, Dec. 9, 1997, Methods and kits using macrophage stimulating protein; Hava Karsenty Avraham, et al., 514/12; 530/351, 380 [IMAGE AVAILABLE]

38. 5,681,719, Oct. 28, 1997, DNA encoding N- and C- terminally truncated colony stimulating factor-1 variants; Martha B. Ladner, et al., 435/69.5, 252.3, 320.1; 530/351; 536/23.5; 930/145 [IMAGE AVAILABLE]

39. 5,681,714, Oct. 28, 1997, Nucleic acid encoding tek receptor tyrosine kinase; Martin L. Breitman, deceased, et al., 435/69.1, 194, 252.3, 254.11, 320.1, 325, 352, 358, 365, 367 [IMAGE AVAILABLE]

40. 5,679,356, Oct. 21, 1997, Use of GM-CSF as a vaccine adjuvant; Eric M. Bonnem, et al., 424/278.1, 209.1, 227.1 [IMAGE AVAILABLE]

41. 5,679,347, Oct. 21, 1997, Methods of isolating CD1-presented antigens, vaccines comprising CD1-presented antigens, and cell lines for use in said methods; Steven A. Porcelli, et al., 424/184.1, 93.71, 185.1, 193.1, 248.1; 435/69.3; 514/2, 23; 530/300, 350, 395, 403 [IMAGE AVAILABLE]

42. 5,677,149, Oct. 14, 1997, Interleukin-3 (IL-3) mutant polypeptides and their recombinant production; S. Christopher Bauer, et al., 435/69.52; 424/85.2; 435/69.51, 69.7; 530/351; 536/23.5; 930/141 [IMAGE AVAILABLE]

43. 5,672,346, Sep. 30, 1997, Human stem cell compositions and methods; Edward Srour, et al., 424/93.7 [IMAGE AVAILABLE]

44. 5,672,343, Sep. 30, 1997, N- 3 deletion mutants of the long form of CSF-1; Martha B. Ladner, et al., 424/85.1; 435/69.5; 530/351 [IMAGE AVAILABLE]

45. 5,670,628, Sep. 23, 1997, Radio-labelling of proteins; Brian Maurice John Foxwell, et al., 530/391.3; 424/178.1; 530/391.9 [IMAGE AVAILABLE]

46. 5,670,146, Sep. 23, 1997, Pharmacological preparations comprising human pluripotent hematopoietic colony stimulating factor; Karl Welte, et al., 424/85.1; 435/69.1, 69.5; 530/350, 351, 395 [IMAGE AVAILABLE]

47. 5,662,896, Sep. 2, 1997, Compositions and methods for cancer immunotherapy; Jack R. Barber, et al., 424/93.2, 93.1; 435/320.1; 514/44 [IMAGE AVAILABLE]

48. 5,662,895, Sep. 2, 1997, Method of administering human pluripotent hematopoietic colony stimulating factor; Karl Welte, et al., 424/85.1; 514/2, 8 [IMAGE AVAILABLE]

49. 5,661,025, Aug. 26, 1997, Self-assembling polynucleotide delivery system comprising dendrimer polycations; Francis C. Szoka, Jr., et al., 435/458, 375; 514/2, 9, 44 [IMAGE AVAILABLE]

50. 5,656,465, Aug. 12, 1997, Methods of in vivo gene delivery; Dennis L. Panicali, et al., 435/456, 320.1 [IMAGE AVAILABLE]

51. 5,656,297, Aug. 12, 1997, Modulated release from biocompatible polymers; Howard Bernstein, et al., 424/484, 486, 487, 488, 489; 514/772.3, 772.6, 781, 805, 935 [IMAGE AVAILABLE]

52. 5,650,501, Jul. 22, 1997, Serine/threonine kinase and nucleic acids encoding same; James W. Dennis, et al., 536/23.2; 435/69.1, 194, 320.1, 325, 348, 352, 358, 365, 367, 419; 530/324, 350; 536/24.1, 24.31 [IMAGE AVAILABLE]

53. 5,650,150, Jul. 22, 1997, Recombinant antibody cytokine fusion proteins; Stephen D. Gillies, 424/134.1, 85.1, 133.1; 435/69.7 [IMAGE AVAILABLE]

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73. 5,591,632, Jan. 7, 1997, Recombinant BCG; Michael A. O'Donnell, et al., 435/252.3, 253.1, 320.1 [IMAGE AVAILABLE]

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91. 5,501,962, Mar. 26, 1996, Interleuken-3 (IL-3) human/murine hybrid polypeptides and recombinant production of the same; Sarah R. Braford-Goldberg, et al., 424/85.2; 435/69.52, 252.3, 254.11, 320.1; 530/351; 536/23.4, 23.5, 24.1 [IMAGE AVAILABLE]

92. 5,496,924, Mar. 5, 1996, Fusion protein comprising an interleukin-2 fragment ballast portion; Paul Habermann, et al., 530/350, 303, 351 [IMAGE AVAILABLE]

93. 5,475,087, Dec. 12, 1995, Antagonists of human granulocyte-macrophage colony stimulating factor derived from the carboxyl terminus; Gail F. Seelig, et al., 530/326, 399 [IMAGE AVAILABLE]

94. 5,463,029, Oct. 31, 1995, Purification of fusion **proteins** comprising **GM**-**CSF** and IL-3; Joseph T. Dunn, et al., 530/416; 435/69.5, 69.52, 69.7, 252.3, 254.11, 320.1; 530/412 [IMAGE AVAILABLE]

95. 5,451,662, Sep. 19, 1995, Method of purifying protein; David Naveh, et al., 530/351, 416 [IMAGE AVAILABLE]

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99. 5,409,825, Apr. 25, 1995, Expansion of human hematopoietic progenitor cells in a liquid medium; Ronald Hoffman, et al., 435/384 [IMAGE AVAILABLE]

100. 5,405,952, Apr. 11, 1995, DNA sequence encoding nonglycosylated analogs of human colony stimulating factors; Michael Deeley, et al., 536/23.5; 435/69.5, 69.9, 235.1, 252.3, 320.1; 530/350 [IMAGE AVAILABLE]

101. 5,393,870, Feb. 28, 1995, Analogs of human granulocyte-macrophage colony stimulating factor; Michael C. Deeley, et al., 530/351; 435/69.1, 69.5, 69.9; 530/395; 930/145 [IMAGE AVAILABLE]

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104. 5,385,901, Jan. 31, 1995, Method of treating abnormal concentrations of TNF .alpha.; Gilla Kaplan, et al., 514/231.5, 231.2, 282, 327, 331, 348 [IMAGE AVAILABLE]

105. 5,376,367, Dec. 27, 1994, Fusion proteins comprising MGF and IL-3; Douglas E. Williams, 424/85.2, 85.1; 435/69.52, 69.7; 530/350, 351, 402 [IMAGE AVAILABLE]

106. 5,362,631, Nov. 8, 1994, C-myb transfected T98G cells which produce GM-CSF and stem cell factor; Bruno Calabretta, 435/69.5, 69.4, 368 [IMAGE AVAILABLE]

107. 5,359,035, Oct. 25, 1994, Bifunctional proteins including interleukin-2 (IL-2) and granuloctyte macrophage colony stimulating factor (GM-CSF); Paul Habermann, 530/351; 424/85.1, 85.2; 530/395, 399, 402, 408, 409, 825; 930/140, 141 [IMAGE AVAILABLE]

108. 5,358,708, Oct. 25, 1994, Stabilization of protein formulations; Suman T. Patel, 424/85.1, 85.2; 530/351 [IMAGE AVAILABLE]

109. 5,358,707, Oct. 25, 1994, Oxidized variants of GM-CSF; Paul Reichert, et al., 424/85.1; 530/351 [IMAGE AVAILABLE]

110. 5,349,052, Sep. 20, 1994, Process for fractionating polyethylene glycol (PEG)-protein adducts and an adduct for PEG and granulocyte-macrophage colony stimulating factor; Cristina Delgado, et al., 530/351, 410, 423 [IMAGE AVAILABLE]

111. 5,298,603, Mar. 29, 1994, **GM**-**CSF** **protein**, its derivatives, the preparation of proteins of this type, and their use; Paul Habermann, et al., 530/351; 435/69.5, 69.52, 69.6; 530/395, 825; 930/140, 144, 145 [IMAGE AVAILABLE]

112. 5,298,395, Mar. 29, 1994, Hyperglycosylated cytokine conjugates; Linda S. Park, 435/7.21, 7.5, 7.8; 436/172, 501, 526 [IMAGE AVAILABLE]

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132. 4,965,344, Oct. 23, 1990, Process for obtaining active proteins from a biologically inactive form; Reinhard Hermann, 530/351; 435/69.1, 69.5; 530/412, 414, 417, 422, 820 [IMAGE AVAILABLE]

133. 4,959,455, Sep. 25, 1990, Primate hematopoietic growth factors IL-3 and pharmaceutical compositions; Steven C. Clark, et al., 530/351; 424/85.1, 85.2; 435/69.52; 530/395, 820, 825, 827 [IMAGE AVAILABLE]

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(FILE 'USPAT' ENTERED AT 11:46:19 ON 06 OCT 1998)
L1 1347 S (GM-CSF OR GRANULOCYTE MACROPHAGE COLONY STIMULATING FAC
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L2 136 S L1 (5A) (PROTEIN? OR POLYPEPTIDE?)
L3 379 S L1 (P) (RECOMBINANT?)

APS search

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> s (GM-CSF or granulocyte macrophage colony stimulating factor or
CSF-alpha or pluripoietin-alpha)
        36977 GM
         2522 CSF
          425 GM-CSF
              (GM(W)CSF)
          882 GRANULOCYTE
         1939 MACROPHAGE
         7816 COLONY
        14889 STIMULATING
       210937 FACTOR
          204 GRANULOCYTE MACROPHAGE COLONY STIMULATING
FACTOR

(GRANULOCYTE(W)MACROPHAGE(W)COLONY(W)STIMULATING(W)FACTO
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)
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       216615 ALPHA
            8 CSF-ALPHA
              (CSF(W)ALPHA)
            2 PLURIPOIETIN
       216615 ALPHA
            0 PLURIPOIETIN-ALPHA
              (PLURIPOIETIN(W)ALPHA)
L1         465 (GM-CSF OR GRANULOCYTE MACROPHAGE COLONY
STIMULATING FACTOR
 OR
              CSF-ALPHA OR PLURIPOIETIN-ALPHA)


=> s l1 (5a) (polypeptide? or protein? or peptide?)
        11419 POLYPEPTIDE?
        59151 PROTEIN?
        19107 PEPTIDE?
L3          54 L1 (5A) (POLYPEPTIDE? OR PROTEIN? OR PEPTIDE?)

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1. 5,525,495, Jun. 11, 1996, Methods and compositions useful in the recognition, binding and expression of ribonucleic acids involved in cell growth, neoplasia and immunoregulation; Jack D. Keene, et al., 435/172.3, 172.1; 530/300, 350; 935/19, 22, 77, 80 [IMAGE AVAILABLE]

2. 5,516,512, May 14, 1996, N- and C-terminal truncation and deletion mutants of human interleukin-3; Lambertus C. J. Dorssers, et al., 424/85.2; 435/69.52; 530/351; 930/141, 145 [IMAGE AVAILABLE]

3. 5,501,962, Mar. 26, 1996, Interleuken-3 (IL-3) human/murine hybrid polypeptides and recombinant production of the same; Sarah R. Braford-Goldberg, et al., 435/69.52; 424/85.2; 435/172.3, 240.2, 252.3, 254.11, 320.1; 530/351; 536/23.4, 23.5, 24.1 [IMAGE AVAILABLE]

4. 5,496,924, Mar. 5, 1996, Fusion protein comprising an interleukin-2 fragment ballast portion; Paul Habermann, et al., 530/350, 303, 351 [IMAGE AVAILABLE]

5. 5,475,087, Dec. 12, 1995, Antagonists of human granulocyte-macrophage colony stimulating factor derived from the carboxyl terminus; Gail F. Seelig, et al., 530/326, 399 [IMAGE AVAILABLE]

6. 5,463,029, Oct. 31, 1995, Purification of fusion **proteins** comprising **GM**-**CSF** and IL-3; Joseph T. Dunn, et al., 530/416; 435/69.5, 69.52, 69.7, 240.1, 252.3, 254.11, 320.1; 530/412 [IMAGE AVAILABLE]

7. 5,451,662, Sep. 19, 1995, Method of purifying protein; David Naveh, et al., 530/351, 416 [IMAGE AVAILABLE]

8. 5,449,755, Sep. 12, 1995, Human cyclin E; James M. Roberts, et al., 530/350, 387.1; 536/23.5 [IMAGE AVAILABLE]

9. 5,444,149, Aug. 22, 1995, Methods and compositions useful in the recognition, binding and expression of ribonucleic acids involved in cell growth, neoplasia and immunoregulation; Jack D. Keene, et al., 530/300, 350 [IMAGE AVAILABLE]

10. 5,422,120, Jun. 6, 1995, Heterovesicular liposomes; Sinil Kim, 424/450; 264/4.1, 4.3, 4.6; 436/829 [IMAGE AVAILABLE]

11. 5,420,105, May 30, 1995, Polymeric carriers for non-covalent drug conjugation; Linda M. Gustavson, et al., 514/2; 424/178.1; 514/8, 387; 530/350, 363, 367, 370, 392, 409; 548/304.1 [IMAGE AVAILABLE]

12. 5,409,825, Apr. 25, 1995, Expansion of human hematopoietic progenitor cells in a liquid medium; Ronald Hoffman, et al., 435/240.1, 240.2, 240.21, 240.25 [IMAGE AVAILABLE]

13. 5,405,952, Apr. 11, 1995, DNA sequence encoding nonglycosylated analogs of human colony stimulating factors; Michael Deeley, et al., 536/23.5; 435/69.5, 69.9, 172.3, 235.1, 252.3, 320.1; 530/350; 935/10, 28, 56, 61, 69 [IMAGE AVAILABLE]

14. 5,393,870, Feb. 28, 1995, Analogs of human granulocyte-macrophage colony stimulating factor; Michael C. Deeley, et al., 530/351; 435/69.1, 69.5, 69.9; 530/395; 930/145 [IMAGE AVAILABLE]

15. 5,391,723, Feb. 21, 1995, Oligonucleotide conjugates; John H. Priest, 536/23.1; 530/402 [IMAGE AVAILABLE]

16. 5,391,706, Feb. 21, 1995, Purification of GM-CSF; Paul P. Trotta, et al., 530/351; 435/69.5; 530/397, 416, 417 [IMAGE AVAILABLE]

17. 5,391,485, Feb. 21, 1995, DNAs encoding analog GM-CSF molecules displaying resistance to proteases which cleave at adjacent dibasic residues; Michael C. Deeley, et al., 435/69.5, 240.1, 254.2, 320.1; 536/23.5 [IMAGE AVAILABLE]

18. 5,385,901, Jan. 31, 1995, Method of treating abnormal concentrations of TNF .alpha.; Gilla Kaplan, et al., 514/231.5, 231.2, 282, 327, 331, 348 [IMAGE AVAILABLE]

19. 5,376,367, Dec. 27, 1994, Fusion proteins comprising MGF and IL-3; Douglas E. Williams, 424/85.2, 85.1; 435/69.52, 69.7; 530/350, 351, 402 [IMAGE AVAILABLE]

20. 5,362,631, Nov. 8, 1994, C-myb transfected T98G cells which produce GM-CSF and stem cell factor; Bruno Calabretta, 435/69.5, 69.4, 240.2 [IMAGE AVAILABLE]

21. 5,359,035, Oct. 25, 1994, Bifunctional proteins including interleukin-2 (IL-2) and granuloctyte macrophage colony stimulating factor (GM-CSF); Paul Habermann, 530/351; 424/85.1, 85.2; 530/395, 399, 402, 408, 409, 825; 930/140, 141 [IMAGE AVAILABLE]

22. 5,358,708, Oct. 25, 1994, Stabilization of protein formulations; Suman T. Patel, 424/85.1, 85.2; 530/351 [IMAGE AVAILABLE]

23. 5,358,707, Oct. 25, 1994, Oxidized variants of GM-CSF; Paul Reichert, et al., 424/85.1; 530/351 [IMAGE AVAILABLE]

24. 5,349,052, Sep. 20, 1994, Process for fractionating polyethylene glycol (PEG)-protein adducts and an adduct for PEG and granulocyte-macrophage colony stimulating factor; Cristina Delgado, et al., 530/351, 410, 423 [IMAGE AVAILABLE]

25. 5,322,678, Jun. 21, 1994, Alteration of pharmacokinetics of proteins by charge modification; Alton C. Morgan, Jr., et al., 424/1.53, 1.49, 178.1, 182.1; 530/391.3, 391.5, 391.7, 402, 410 [IMAGE AVAILABLE]

26. 5,298,603, Mar. 29, 1994, **GM**-**CSF** **protein**, its derivatives, the preparation of proteins of this type, and their use; Paul Habermann, et al., 530/351; 435/69.5, 69.52, 69.6; 530/395, 825; 930/140, 144, 145 [IMAGE AVAILABLE]

27. 5,298,395, Mar. 29, 1994, Hyperglycosylated cytokine conjugates; Linda S. Park, 435/7.21, 7.5, 7.8; 436/172, 501, 526 [IMAGE AVAILABLE]

28. 5,256,648, Oct. 26, 1993, Selective inhibition of gene expression by photoactivatable oligonucleotides; Francis P. Gasparro, et al., 514/44; 435/172.3; 514/455; 536/24.5 [IMAGE AVAILABLE]

29. 5,252,713, Oct. 12, 1993, Polymeric carriers for non-covalent drug conjugation; Alton C. Morgan, Jr., et al., 530/391.7; 424/178.1; 435/188; 530/350, 351, 362, 363, 391.9, 392, 399, 402 [IMAGE AVAILABLE]

30. 5,242,687, Sep. 7, 1993, Method of reducing cellular immune response involving T-cells using CD8-bearing antigen presenting cells; Mark L. Tykocinski, et al., 424/184.1, 93.71, 178.1, 278.1; 435/252.3; 514/2, 8, 885; 530/402, 403, 866, 868 [IMAGE AVAILABLE]

31. 5,229,496, Jul. 20, 1993, Analogs of human granulocyte-macrophage

colony stimulating factor; Michael C. Deeley, et al., 530/351; 435/69.1, 69.5, 69.9; 530/395; 930/145 [IMAGE AVAILABLE]

32. 5,217,881, Jun. 8, 1993, Hyperglycosylated cytokine conjugates; Linda S. Park, 435/69.5, 7.5, 7.9, 69.51, 69.52, 174, 188, 964; 436/518, 544, 545, 546; 530/351, 395, 810 [IMAGE AVAILABLE]

33. 5,200,327, Apr. 6, 1993, Expression system for the secretion of bioactive human **granulocyte** **macrophage** **colony** **stimulating** **factor** (**GM**-**CSF**) and other heterologous **proteins** from streptomyces; Robert T. Garvin, et al., 435/69.5, 69.1, 172.3, 252.3, 320.1; 530/399; 536/23.5; 935/48, 60 [IMAGE AVAILABLE]

34. 5,199,942, Apr. 6, 1993, Method for improving autologous transplantation; Steven Gillis, 604/4; 128/898; 424/85.2, 529; 435/240.21; 604/49 [IMAGE AVAILABLE]

35. 5,171,675, Dec. 15, 1992, Macrophage colony stimulating factor-.gamma.; Douglas P. Cerretti, et al., 435/69.5, 320.1; 530/399 [IMAGE AVAILABLE]

36. 5,162,111, Nov. 10, 1992, Treatment of bacterial diseases with granulocyte-macrophage colony stimulating factor; Kenneth H. Grabstein, et al., 424/85.1; 435/320.1; 514/2, 8; 530/351, 395; 536/23.5, 23.51; 930/145 [IMAGE AVAILABLE]

37. 5,128,450, Jul. 7, 1992, Nonglycosylated human interleukin-3 analog proteins; David L. Urdal, et al., 530/351; 424/85.1, 85.2; 435/69.52; 530/824; 930/141; 935/49, 50 [IMAGE AVAILABLE]

38. 5,112,961, May 12, 1992, DNA encoding subunits of a high affinity GM-CSF receptor; Kazuhiro Hayashida, et al., 536/23.51; 435/69.1, 69.5; 530/350, 351 [IMAGE AVAILABLE]

39. 5,109,119, Apr. 28, 1992, Crystalline r-h-GM-CSF and method; Paul Reichert, et al., 530/402; 435/69.5; 530/351, 410, 412, 414, 417, 418, 419, 420, 421, 422; 930/145 [IMAGE AVAILABLE]

40. 5,108,910, Apr. 28, 1992, DNA sequences encoding fusion **proteins** comprising **GM**-**CSF** and IL-3; Benson M. Curtis, et al., 435/69.7, 69.5, 69.52, 172.3, 320.1; 536/23.4, 23.51 [IMAGE AVAILABLE]

41. 5,106,733, Apr. 21, 1992, Bovine granulocyte-macrophage colony stimulating factor; Paul E. Baker, et al., 435/69.5, 240.1, 243, 320.1; 536/23.51, 24.1 [IMAGE AVAILABLE]

42. 5,104,650, Apr. 14, 1992, Uses of recombinant colony stimulating factor-1; Peter Ralph, et al., 424/85.1, 85.2, 85.4, 85.5, 85.6; 514/885, 889 [IMAGE AVAILABLE]

43. 5,078,996, Jan. 7, 1992, Activation of macrophage tumoricidal activity by granulocyte-macrophage colony stimulating factor; Paul J. Conlon, III, et al., 424/85.1, 93.71, 534; 435/69.5, 172.2, 172.3; 514/2, 8, 21; 530/350, 351, 828; 536/23.5, 23.51 [IMAGE AVAILABLE]

44. 5,073,627, Dec. 17, 1991, Fusion **proteins** comprising **GM**-**CSF** and IL-3; Benson M. Curtis, et al., 530/351; 435/69.5, 69.52, 69.7; 530/402, 403, 404, 405, 808 [IMAGE AVAILABLE]

45. 5,070,013, Dec. 3, 1991, Immunochemical assay for human granulocyte-macrophage colony stimulating factor; John S. Abrams, et al., 435/7.5, 7.9, 7.94, 18, 21, 28, 172.2, 240.27, 975; 436/501, 518, 536, 548, 808, 824; 530/388.23, 413, 809; 935/95, 106, 110 [IMAGE AVAILABLE]

46. 5,047,504, Sep. 10, 1991, Method for purifying granulocyte-macrophage colony stimulating factor; Thomas C. Boone, 530/351; 435/69.1, 69.5; 530/395, 412, 416, 417, 418, 419, 420, 820 [IMAGE AVAILABLE]

47. 5,032,676, Jul. 16, 1991, Nonglycosylated analogs of human colony stimulating factors; Michael Deeley, et al., 530/351; 435/69.1, 69.5, 69.6; 530/350, 395, 820, 824; 935/49, 50 [IMAGE AVAILABLE]

48. 5,011,912, Apr. 30, 1991, Hybridoma and monoclonal antibody for use in an immunoaffinity purification system; Thomas P. Hopp, et al., 530/387.9; 435/70.21, 240.27 [IMAGE AVAILABLE]

49. 4,987,121, Jan. 22, 1991, Erythropoietic factor; Alex J. Baertschi, et al., 514/8, 12, 13; 530/397 [IMAGE AVAILABLE]

50. 4,965,344, Oct. 23, 1990, Process for obtaining active proteins from a biologically inactive form; Reinhard Hermann, 530/351; 435/69.1, 69.5; 530/412, 414, 417, 422, 820 [IMAGE AVAILABLE]

51. 4,959,455, Sep. 25, 1990, Primate hematopoietic growth factors IL-3 and pharmaceutical compositions; Steven C. Clark, et al., 530/351; 424/85.1, 85.2; 435/69.52; 530/395, 820, 825, 827 [IMAGE AVAILABLE]

52. 4,877,729, Oct. 31, 1989, Recombinant DNA encoding novel family of primate hematopoietic growth factors; Steven C. Clark, et al., 435/69.52, 69.5, 172.3, 240.2, 252.33, 320.1; 935/9, 10, 11, 13 [IMAGE AVAILABLE]

53. 4,868,119, Sep. 19, 1989, Hematopoietic growth factors; Steven C. Clark, et al., 435/240.2, 172.3, 252.31, 252.33, 320.1; 536/23.51, 24.1; 930/120; 935/9, 11, 13 [IMAGE AVAILABLE]

54. 4,851,341, Jul. 25, 1989, Immunoaffinity purification system; Thomas P. Hopp, et al., 435/69.7, 172.3, 240.27; 530/387.9; 930/10, 145, 300; 935/95, 104, 108 [IMAGE AVAILABLE]

stn/cas search

> s (GM-CSF or granulocyte macrophage colony stimulating factor or CSF-alpha or pluripoietin-alpha)

16380 GM
25626 CSF
4948 GM-CSF
(GM(W)CSF)
17469 GRANULOCYTE
37985 MACROPHAGE
39140 COLONY
49856 STIMULATING
292280 FACTOR
6434 GRANULOCYTE MACROPHAGE COLONY STIMULATING FACTOR

(GRANULOCYTE(W)MACROPHAGE(W)COLONY(W)STIMULATING(W)FACTOR)
25626 CSF
265659 ALPHA
41 CSF-ALPHA
(CSF(W)ALPHA)
12 PLURIPOIETIN
265659 ALPHA
4 PLURIPOIETIN-ALPHA
(PLURIPOIETIN(W)ALPHA)
L1 7516 (GM-CSF OR GRANULOCYTE MACROPHAGE COLONY STIMULATING FACTOR OR CSF-ALPHA OR PLURIPOIETIN-ALPHA)

=> s l1 (5a) (protein? or polypeptide? or peptide?)

831076 PROTEIN?
58548 POLYPEPTIDE?
213320 PEPTIDE?

L2 302 L1 (5A) (PROTEIN? OR POLYPEPTIDE? OR PEPTIDE?)

=> d l2 200-302 bib ab

L2 ANSWER 200 OF 302 MEDLINE
AN 92088969 MEDLINE
TI The network of hemopoietic regulatory proteins in myeloid cell differentiation.
AU Lotem J; Shabo Y; Sachs L
CS Department of Molecular Genetics and Virology, Weizmann Institute of Science, Rehovot, Israel..
SO CELL GROWTH AND DIFFERENTIATION, (1991 Sep) 2 (9) 421-7.
Journal code: AYH. ISSN: 1044-9523.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 9204
AB There are clones of myeloid leukemic cells that can be induced to undergo terminal cell differentiation to macrophages by normal hemopoietic regulatory proteins. Induction of differentiation in two different clones of myeloid leukemic cells with interleukin 6 (IL-6) or granulocyte-macrophage colony-stimulating factor (GM-CSF) resulted in induction of mRNA for the hemopoietic regulatory ***proteins*** IL-6, ***GM*** - ***CSF*** , interleukin 1 alpha and interleukin 1 beta, tumor necrosis factor, and transforming growth factor beta 1. In one of these clones, induction of differentiation with GM-CSF was also associated with induction of mRNA for macrophage colony-stimulating factor (M-CSF) but not for the receptor for M-CSF (c-fms), whereas in the other clone, induction of differentiation with IL-6 was associated with induction of mRNA for both c-fms and M-CSF. The clones also differed in their responsiveness to these regulators. There was no induction of mRNA for granulocyte colony-stimulating factor or interleukin 3 during differentiation of either clone. The results indicate that the genes for a nearly normal network of positive and negative hemopoietic regulatory proteins are induced during differentiation of these myeloid leukemic cells and that there are leukemic clones with specific defects in this network.

L2 ANSWER 201 OF 302 MEDLINE
AN 92043765 MEDLINE
TI IL-1, IL-4, and IFN-gamma differentially regulate cytokine production and cell surface molecule expression in cultured human thymic epithelial cells.
AU Galy A H; Spits H
CS DNAX Research Institute, Palo Alto, CA 94304..
SO JOURNAL OF IMMUNOLOGY, (1991 Dec 1) 147 (11) 3823-30.
Journal code: IFB. ISSN: 0022-1767.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Abridged Index Medicus Journals; Priority Journals; Cancer Journals
EM 9202
AB We investigated the response of purified and cloned human thymic epithelial cells (TEC) to IL-1, IL-4, and IFN-gamma stimulation in vitro. IL-1 alpha strongly up-regulated the production of granulocyte-macrophage CSF (GM-CSF), granulocyte CSF (G-CSF), IL-6, and IL-8, as measured by specific immunoenzymetric assays and by increased steady state mRNA levels. IL-4 or IFN-gamma did not induce these cytokines in TEC but in a sustained and dose-dependent manner down-regulated the IL-1-induced ***GM*** - ***CSF*** ***protein*** and mRNA levels. Only IFN-gamma, and not IL-4, suppressed the IL-1-induced G-CSF and IL-8 production, as shown at both the protein and mRNA levels. The inhibition was dose dependent, sustained for at least 96 h, and more pronounced for G-CSF than for IL-8. In contrast, both IL-4 and IFN-gamma enhanced the IL-1-induced IL-6 production. IL-4 and IFN-gamma had additive effects to increase IL-6 secretion and to more completely suppress the IL-1-induced GM-CSF. Analyses of cell surface molecules showed that intercellular adhesion molecule 1 (ICAM-1) expression on TEC was increased by IL-1 or IFN-gamma. IL-4 slightly down-regulated constitutive ICAM-1 levels but did not significantly modify the levels of expression induced by either IL-1 or IFN-gamma. MHC class II expression was induced by IFN-gamma but not by IL-1 or IL-4. The combination of IL-1 and IL-4 with IFN-gamma did not alter the levels of class II MHC Ag induced by IFN-gamma. In conclusion, TEC cytokine production and cell surface molecule expression are differentially regulated via a complex cytokine network. Our data suggest that developing T cells provide, in part, the signals controlling the function of their supporting stroma.

L2 ANSWER 202 OF 302 MEDLINE
AN 92039663 MEDLINE
TI A neutralizing monoclonal antibody binds to an epitope near the amino terminus of murine granulocyte-macrophage colony-stimulating factor.
AU Meropol N J; Kreider B L; Lee V M; Kaushansky K; Prystowsky M B
CS Hematology-Oncology Section, Hospital of the University of Pennsylvania, Philadelphia 19104..
NC CA48648 (NCI)
HL08268-01 (NHLBI)
SO HYBRIDOMA, (1991 Aug) 10 (4) 433-47.
Journal code: GFS. ISSN: 0272-457X.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 9202
AB A rat anti-murine granulocyte-macrophage colony-stimulating factor (mGM-CSF) monoclonal antibody, A2, that neutralizes bioactivity in vitro was isolated. The binding epitope recognized by this antibody was identified using human-murine hybrid ***GM*** - ***CSF*** ***proteins*** . A2 was unable to immunoprecipitate a hybrid (hm7) ***protein*** containing the human ***GM*** - ***CSF*** sequence for the first 11 amino terminal amino acids, and the mGM-CSF sequence for amino acids 12-124. In contrast, A2 did recognize a hybrid which substitutes human GM-CSF amino acids 23-36 in the murine sequence. These data suggest that this neutralizing antibody recognizes an epitope at the amino terminus of mGM-CSF. Because hm7 did maintain in vitro bioactivity, it is probable that the epitope recognized by the neutralizing antibody is not itself part of the receptor-binding domain of mGM-CSF; rather, it is likely that neutralization occurs as a result of antibody binding near the receptor-binding site, with steric inhibition of mGM-CSF binding to its receptor. Interestingly, monoclonal antibody A2 does not recognize mGM-CSF glycosylation species corresponding to predicted maximal O-glycosylation variants. The presence of O-glycosylation sites within the antibody-binding epitope was confirmed using site-directed mutagenesis. Potential O-glycosylation sites in native mGM-CSF were removed by introducing conservative amino acid substitutions, and expected molecular weight reductions were obtained. These findings are consistent with previous reports that suggest the importance of the integrity of residues near the amino terminus to GM-CSF bioactivity.

L2 ANSWER 203 OF 302 MEDLINE
AN 92039044 MEDLINE
TI Cloning and expression of a cDNA encoding ovine granulocyte-macrophage colony-stimulating factor.
AU McInnes C J; Haig D M
CS Moredun Research Institute, Edinburgh, U.K..
SO GENE, (1991 Sep 15) 105 (2) 275-9.
Journal code: FOP. ISSN: 0378-1119.
CY Netherlands
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
OS GENBANK-X53561; GENBANK-S63416; GENBANK-X55680; GENBANK-M63989;
GENBANK-M63990; GENBANK-S61507; GENBANK-M59725; GENBANK-M59726;
GENBANK-M59727; GENBANK-M59728
EM 9202
AB A cDNA encoding ovine granulocyte-macrophage colony-stimulating factor (GM-CSF) has been cloned using the polymerase chain reaction. The nucleotide sequence is approx. 93% identical to the published bovine GM-CSF-encoding sequence, 84% to the human sequence and 73% to the murine sequence. The deduced amino acid sequence of the ovine ***GM*** - ***CSF*** ***protein*** was found to be 80% identical to both the human and bovine proteins and 57% to the murine ***protein*** . Transient expression of recombinant ovine ***GM*** - ***CSF*** in COS-1 cells was obtained and its biological activity investigated in a bone-marrow colony-forming assay. Ovine GM-CSF was found to promote the formation of granulocyte-macrophage colonies as well as eosinophil, neutrophil and monocyte/macrophage colonies, an activity characteristic of GM-CSF in other species. Recombinant human GM-CSF was found to have no proliferative effect on ovine bone-marrow cells.

L2 ANSWER 204 OF 302 MEDLINE
AN 92012670 MEDLINE
TI Episodic eosinophilia-myalgia-like syndrome in a patient without L-tryptophan use: association with eosinophil activation and increased serum levels of granulocyte-macrophage colony-stimulating factor [see comments].
CM Comment in: J Allergy Clin Immunol 1992 May;89(5):1064
AU Bochner B S; Friedman B; Krishnaswami G; Schleimer R P; Lichtenstein L M; Kroegel C
CS Department of Medicine, Johns Hopkins Asthma and Allergy Center, Baltimore, MD 21224..
NC AI27429 (NIAID)
AI08270 (NIAID)
AI20136 (NIAID)
SO JOURNAL OF ALLERGY AND CLINICAL IMMUNOLOGY, (1991 Oct) 88 (4)
629-36.
Journal code: H53. ISSN: 0091-6749.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Abridged Index Medicus Journals; Priority Journals
EM 9201
AB We have studied a patient with recurrent bouts of angioedema, myalgia, and eosinophilia that was not due to L-tryptophan ingestion. Peripheral blood eosinophils (EOSs) during exacerbations of his illness displayed characteristics of "activation," including hypodense phenotype and increased responsiveness to platelet-activating factor (PAF) in vitro with respect to expression of CD11b surface adhesion ***proteins*** . Elevated serum levels of ***granulocyte*** - ***macrophage*** ***colony*** - ***stimulating*** ***factor*** (GM-CSF) bioactivity were also detected, whereas interleukin-3 and interleukin-5 levels were not increased. During treatment with glucocorticoids, all clinical symptoms resolved, EOSs decreased in number and became normodense, PAF responsiveness diminished, and GM-CSF levels returned to normal. During glucocorticoid tapering, a subsequent clinical relapse was again associated with EOS hypodensity, increased PAF responsiveness, and increased serum GM-CSF levels. Although this patient satisfies the diagnostic criteria for eosinophilia-myalgia syndrome, the episodic and profound nature of exacerbations and response to therapy in the absence of L-tryptophan usage suggests a possible overlap with the syndrome of episodic angioedema and eosinophilia. In vitro studies suggest that GM-CSF may play a role in the eosinophilia, EOS activation, and pathophysiology of disease in this patient and demonstrate resolution of these abnormalities during glucocorticoid therapy. The efficacy of glucocorticoid therapy in some hypereosinophilic states may therefore be mediated, at least in part, via reduction of GM-CSF production and/or EOS activation.

L2 ANSWER 205 OF 302 MEDLINE
AN 92003953 MEDLINE
TI Role of AUUU sequences in stabilization of granulocyte-macrophage colony-stimulating factor RNA in stimulated cells.
AU Akashi M; Shaw G; Gross M; Saito M; Koeffler H P
CS Center for Health Sciences, UCLA School of Medicine 90024-1678..
NC CA 26038 (NCI)
CA 33936 (NCI)
CA 42710 (NCI)
SO BLOOD, (1991 Oct 15) 78 (8) 2005-12.
Journal code: A8G. ISSN: 0006-4971.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Abridged Index Medicus Journals; Priority Journals; Cancer Journals
EM 9201
AB RNAs for transiently expressed genes such as oncogenes and cytokines, including granulocyte-monocyte colony-stimulating factor (GM-CSF), have a short half-life (T1/2). A cluster of AUUU sequences identified in the 3' untranslated (UT) region of these RNAs has been implicated in controlling stability of these transcripts. We examined the role of AUUU sequences in mRNA stability of GM-CSF after stimulation of cells. Human fibroblasts (W138) were stably transfected with chimeric constructs containing the beta-globin gene linked to a 52-bp tail of GM-CSF containing either eight ATTTT (pNEOR beta G-AT) or eight repeats in which the AT sequences have been changed to GC sequences (pNEOR beta G-GC). Data confirmed that AUUU sequences in 3'UT region of GM-CSF play a major role in ***GM*** - ***CSF*** RNA instability. Stimulators of ***protein*** kinase C (PKC), cycloheximide (CHX), sodium fluoride (NaF), and, to a more limited extent, interleukin-1 beta (IL-1 beta), appear to stabilize GM-CSF RNA through these AUUU sequences, but tumor necrosis factor-alpha (TNF-alpha) induces stabilization of GM-CSF RNA through a mechanism independent of their AUUU sequences.

L2 ANSWER 206 OF 302 MEDLINE
AN 92000505 MEDLINE
TI The dendritic cell system and its role in immunogenicity.
AU Steinman R M
CS Laboratory of Cellular Physiology and Immunology, Rockefeller University, New York, New York 10021..
NC AI13013 (NIAID)
AI24540 (NIAID)
AI24775 (NIAID)
SO ANNUAL REVIEW OF IMMUNOLOGY, (1991) 9 271-96. Ref: 136
Journal code: ALO. ISSN: 0732-0582.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, ACADEMIC)
LA English
FS Priority Journals
EM 9201
AB Dendritic cells are a system of antigen presenting cells that function to initiate several immune responses such as the sensitization of MHC-restricted T cells, the rejection of organ transplants, and the formation of T-dependent antibodies. Dendritic cells are found in many nonlymphoid tissues but can migrate via the afferent lymph or the blood stream to the T-dependent areas of lymphoid organs. In skin, the immunostimulatory function of dendritic cells is enhanced by cytokines, especially ***GM*** - ***CSF*** . After foreign ***proteins*** are administered in situ, dendritic cells are a principal reservoir of immunogen. In vitro studies indicate that dendritic cells only process proteins for a short period of time, when the rate of synthesis of MHC products and content of acidic endocytic vesicles are high. Antigen processing is selectively dampened after a day in culture, but the capacity to stimulate responses to surface bound peptides and mitogens remains strong. Dendritic cells are motile, and efficiently cluster and activate T cells that are specific for stimuli on the cell surface. High levels of MHC class-I and -II products and several adhesins, such as ICAM-1 and LFA-3, likely contribute to these functions. Therefore dendritic cells are specialized to mediate several physiologic components of immunogenicity such as the acquisition of antigens in tissues, the migration to lymphoid organs, and the identification and activation of antigen-specific T

cells. The function of these presenting cells in immunologic tolerance is just beginning to be studied.

L2 ANSWER 207 OF 302 MEDLINE
AN 91372318 MEDLINE
TI Biological effects of recombinant erythropoietin, granulocyte-macrophage colony-stimulating factor, interleukin 3, and interleukin 6 on purified rat megakaryocytes.
AU Ishida Y; Yano S; Yoshida T; Tanaka H; Yamada Y; Kawano M; Kaneko T;
Matsumoto N
CS Third Department of Internal Medicine, Yamaguchi University School of Medicine, Japan..
SO EXPERIMENTAL HEMATOLOGY, (1991 Aug) 19 (7) 608-12.
Journal code: EPR. ISSN: 0301-472X.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
EM 9112
AB The biological effects of recombinant hematopoietic factors, which are considered to stimulate megakaryocytopoiesis in vitro or in vivo, were studied utilizing purified rat megakaryocytes. Recombinant human erythropoietin (rhEPO), recombinant murine granulocyte-macrophage colony-stimulating factor (rmGM-CSF), and recombinant murine interleukin 3 (rmIL-3) stimulated both [3H]thymidine and [3H]leucine incorporation into purified rat megakaryocytes. In contrast, recombinant human interleukin 6 (rhIL-6) did not stimulate [3H]thymidine uptake but did increase [3H]leucine incorporation into purified rat megakaryocytes. These in vitro data suggest that DNA synthesis in megakaryocytes may be regulated by EPO, ***GM*** - ***CSF*** , and IL-3, and that ***protein*** synthesis is stimulated by EPO, ***GM*** - ***CSF*** , IL-3, and IL-6 in vitro.

L2 ANSWER 208 OF 302 MEDLINE
AN 91359729 MEDLINE
TI Screening for expression of cytokines with hematopoietic growth factor activity by permanent human B-cell lines.
AU Lindemann A; Dorken B; Henschler R; Mertelsmann R; Herrmann F
CS Department of Internal Medicine I (Hematology and Oncology), University of Freiburg Medical Center, Germany..
SO LEUKEMIA, (1991 Aug) 5 (8) 715-8.
Journal code: LEU. ISSN: 0887-6924.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
EM 9112
AB Using colony assays in semi-solid media, several investigators have shown that supernatants (SN) of normal and malignant human B-cells can stimulate the growth of granulocyte-macrophage (GM) progenitor cells. So far macrophage colony-stimulating factor (M-CSF) and interleukin-6 (IL-6) have been identified as potential colony-stimulating activity (CSA) present in B-cell SN. However, other CSAs such as GM-CSF, G-CSF, IL-1-beta, IL-3, and IL-4 may also be candidates in this respect. Several human B-cell lines (CL) were screened for the expression of the respective genes at the mRNA and ***protein*** level. Constitutive production of ***GM*** - ***CSF*** was detected in the lymphoblastoid CL Wi-L2-729-HF2 and in the Burkitt line Raji. The signal intensity of specific transcripts and the amount of protein being secreted increased upon exposure to the phorbol ester PMA. The hybridoma line HB-564 also expressed the GM-CSF gene, but required prior stimulation with PMA. 3H-thymidine incorporation of Raji and Wi-L2-729-HF2 cells was unchanged in the presence or absence of a specific neutralizing sheep anti-GM-CSF serum, suggesting that GM-CSF did not serve as an extracellular autocrine growth factor. The expression of the GM-CSF gene was independent of the proliferative state (log phase growth versus plateau phase growth) and of the presence of serum in cultures of the respective CL. The expression of G-CSF, IL-1-beta, IL-3, and IL-4 genes was not detectable in the CL at the mRNA level.

L2 ANSWER 209 OF 302 MEDLINE
AN 91317887 MEDLINE
TI GM-CSF and phorbol esters modulate GM-CSF receptor expression by independent mechanisms.
AU Brizzi M F; Arduino C; Avanzi G C; Bussolino F; Pegoraro L
CS Dipartimento di Scienze Biomediche e Oncologia Umana, Universita di Torino, Italy..
SO JOURNAL OF CELLULAR PHYSIOLOGY, (1991 Jul) 148 (1) 24-34.
Journal code: HNB. ISSN: 0021-9541.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
EM 9111
AB Human granulocyte-macrophage colony-stimulating factor (GM-CSF) (0.1 nM) down-modulates its receptor in IL-3/GM-CSF dependent M-07e cells, in KG-1 cells and normal granulocytes, whereas phorbol esters 12-O-tetradecanoylphorbol-13-acetate (TPA) (2 nM) down-modulates the GM-CSF receptor in M-07e cells and granulocytes but not in KG-1 cells. As data analysis shows by nonlinear regression, the decreased binding ability depends on a reduction of the binding sites with no significant change of their dissociation constant. To gain insight into the mechanisms involved in the GM-CSF receptor regulation, we investigated the role of ***protein*** kinase C (PKC). ***GM*** - ***CSF*** , unlike TPA, was unable to activate PKC in all the cells studied. Moreover, unlike TPA, GM-CSF was still able to down-modulate its receptor in cells where PKC was inhibited by 1-(5-Isoquinolonesulphonyl)-2-methylpiperazine (H7) and staurosporine or in cells where PKC was exhausted by prolonged incubation with 1 microM TPA. Finally, the receptor re-expression rate was accelerated by protein kinases inhibitors. These results, taken together, indicate the presence of a PKC-dependent and -independent down-modulation mechanism and a negative role of the endogeneous ***protein*** kinases in ***GM*** - ***CSF*** receptor re-expression.

L2 ANSWER 210 OF 302 MEDLINE
AN 91316272 MEDLINE
TI Identification and characterization of a low-affinity granulocyte-macrophage colony-stimulating factor receptor on primary and cultured human melanoma cells.
AU Baldwin G C; Golde D W; Widhopf G F; Economou J; Gasson J C
CS Department of Medicine, Jonsson Comprehensive Cancer Center, Los Angeles, CA..
NC CA30388 (NCI)
CA32737 (NCI)
CA40163 (NCI)
+
SO BLOOD, (1991 Aug 1) 78 (3) 609-15.
Journal code: A8G. ISSN: 0006-4971.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Abridged Index Medicus Journals; Priority Journals; Cancer Journals
EM 9111
AB Hematopoietic growth factor receptors are present on cells of normal nonhematopoietic tissues such as endothelium and placenta. We previously demonstrated functional human granulocyte-macrophage colony-stimulating factor (GM-CSF) receptors on small cell carcinoma of the lung cell lines, and others have reported that certain solid tumor cell lines respond to GM-CSF in clonogenic assays. In the current study, we examine human melanoma cell lines and fresh specimens of melanoma to determine whether they have functional GM-CSF receptors. Scatchard analyses of 125I-GM-CSF equilibrium binding to melanoma cell lines showed a mean of 542 +/- 67 sites per cell with a kd of 0.72 +/- 0.14 nmol/L. Cross-linking studies in the melanoma cell line, M14, showed a major GM-CSF receptor species of 84,000 daltons. Under the conditions tested, the M14 cells did not have a proliferative response to GM-CSF in vitro, nor was any induction of primary response genes detected by Northern analysis in response to GM-CSF. Studies to determine internal translocation of the receptor-ligand complex indicated less than 10% of the 125I-GM-CSF internalized was specifically bound to receptors. Primary melanoma cells from five surgical specimens had GM-CSF receptors; Scatchard analysis was performed on one sample, showing 555 sites/cell with a kd of 0.23 nmol/L. These results indicate that human tumor cells may express a low-affinity ***GM*** - ***CSF*** receptor ***protein*** that localizes to the cell surface and binds ligand, but lacks functional components or accessory factors needed to transduce a signal.

L2 ANSWER 211 OF 302 MEDLINE
AN 91311304 MEDLINE
TI CD45 cell surface antigens are linked to stimulation of early human myeloid progenitor cells by interleukin 3 (IL-3), granulocyte/macrophage colony-stimulating factor (GM-CSF), a ***GM*** - ***CSF*** /IL-3 fusion ***protein*** , and mast cell growth factor (a c-kit ligand).
AU Broxmeyer H E; Lu L; Hangoc G; Cooper S; Hendrie P C; Ledbetter J A;

Xiao M; Williams D E; Shen F W
CS Department of Medicine Hematology/Oncology, Indiana University School of Medicine, Indianapolis 46202..
NC R37 CA-36464 (NCI)
RO1 CA-36740 (NCI)
SO JOURNAL OF EXPERIMENTAL MEDICINE, (1991 Aug 1) 174 (2) 447-58.
Journal code: I2V. ISSN: 0022-1007.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
EM 9110
AB CD45 antigens are protein tyrosine phosphatases. A possible link was evaluated between expression of CD45 antigens on human myeloid progenitor cells (MPC) (colony-forming unit-granulocyte/macrophage [CFU-GM], burst-forming unit-erythroid [BFU-E], and colony-forming unit-granulocyte/erythroid/macrophage/megakaryocyte [CFU-GEMM]) and regulation of MPC by colony-stimulating factors (CSF) (interleukin 3 [IL-3], GM-CSF, G-CSF, M-CSF, and erythropoietin [Epo]), a ***GM*** - ***CSF*** /IL-3 fusion ***protein*** , and mast cell growth factor (MGF; a c-kit ligand). Treatment of cells with antisense oligodeoxynucleotides (oligos) to exons 1 and 2, but not 4, 5, or 6, of the CD45 gene, or with monoclonal anti-CD45, significantly decreased CFU-GM colony formation stimulated with ***GM*** - ***CSF*** , IL-3, fusion ***protein*** , and ***GM*** - ***CSF*** + MGF, but not with G-CSF or M-CSF. It also decreased ***GM*** - ***CSF*** , IL-3, fusion ***protein*** , and MGF-enhanced Epo-dependent BFU-E and CFU-GEMM colony formation, but had little or no effect on BFU-E or CFU-GEMM colony formation stimulated by Epo alone. Similar results were obtained with unseparated or purified (greater than or equal to one of two cells being a MPC) bone marrow cells. Sorted populations of CD343+ HLA-DR+ marrow cells composed of 90% MPC were used to demonstrate capping of CD45 after crosslinking protocols. Also, a decreased percent of CD45+ cells and CD45 antigen density was noted after treatment of column-separated CD34+ cells with antisense oligos to exon 1 of the CD45 gene. These results demonstrate that CD45 cell surface antigens are linked to stimulation of early human MPC by IL-3, GM-CSF, a ***GM*** - ***CSF*** /IL-3 fusion ***protein*** , and MGF.

L2 ANSWER 212 OF 302 MEDLINE
AN 91310659 MEDLINE
TI Identification of critical amino acid residues in human and mouse granulocyte-macrophage colony-stimulating factor and their involvement in species specificity.
AU Shanafelt A B; Johnson K E; Kastelein R A
CS Department of Molecular Biology, DNAX Research Institute of Molecular and Cellular Biology, Palo Alto, California 94304-1104..
SO JOURNAL OF BIOLOGICAL CHEMISTRY, (1991 Jul 25) 266 (21) 13804-10.
Journal code: HIV. ISSN: 0021-9258.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
EM 9110
AB Segments critical to the activity of human granulocyte-macrophage colony-stimulating factor (GM-CSF) were identified by scanning deletion analysis and compared with the critical regions previously identified in the homologous mouse ***GM*** - ***CSF*** ***protein*** . Three of the four critical regions thus identified are in equivalent positions in their respective polypeptides, while a fourth critical region of each is uniquely located. To investigate whether unique critical regions are responsible for the observed species specificity of human and mouse GM-CSF, all critical regions were substituted into their opposite homologue. This identified one specific, but different, critical region in each homologue that could not be replaced. Further characterization of the nature of the species specificity of these two proteins was accomplished by the generation of a series of human/mouse ***GM*** - ***CSF*** hybrids. Each hybrid ***protein*** was assayed for specific activity on human- and mouse GM-CSF-dependent cell lines. Significant differences in the specific activity of these hybrids was observed, suggesting that different segments of each molecule interact with their respective receptors. Based on these two approaches, individual amino acids were identified that could provide, at least in part, the interactions between these protein ligands and their respective receptors. These residues are Thr-78 and Met-80 in human GM-CSF and Asp-92, Thr-98, and Asp-102 in mouse GM-CSF.

L2 ANSWER 213 OF 302 MEDLINE
AN 91309266 MEDLINE
TI Macrophages and migratory cells in endometrium relevant to implantation.
AU Lea R G; Clark D A
SO BAILLIERES CLINICAL OBSTETRICS AND GYNAECOLOGY, (1991 Mar) 5 (1)
25-59. Ref: 181
Journal code: DFO. ISSN: 0950-3552.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LA English
FS Priority Journals
EM 9110
AB The implantation of an appropriately developed embryo into a suitably conditioned uterine lining depends on the synchronous maturation of the preimplantation embryo and uterine lining. The pre- and postimplantation embryo also requires protection from immunocompetent maternal immune effectors. Preimplantation embryo development is affected by genotype, intercellular communication and autocrine growth factors (polyamines, TGF-alpha, TGF-beta 1, PAF). Factors of maternal origin may also enhance embryo development (EGF, TGF-alpha, TGF-beta 1, IGF, polyamines). The preimplantation embryo signals its presence to the mother by release of factor(s) such as IFN-alpha-II and a PAF-like factor. PAF may induce EPF in the mother and enhances vascular permeability at the implantation site. Uterine or peritoneal leukocytosis may inhibit development via toxic effects of lymphokines/monokines (IL-2, IL-1?, IFN-gamma, TNF-alpha). Immunoprotection of the preimplantation embryo is conferred by embryo derived maternal factors (EPF, T-cell suppressor factors). The uterus is receptive during a limited period of time (implantation window) and the substrate adhesion molecules produced by uterine and embryonic trophectoderm cells are crucial for the initial stages of implantation. At implantation, trophoblast expression of MHC and non-MHC antigens is shut off and both immunocompetent maternal cells (macrophages, dendritic cells, granulocytes, IELs, immunocytes) and lymphatics become sparse at implantation sites. Peri-implantation cytokines of maternal origin, such as CSF-1, ***GM*** - ***CSF*** and IGF-1 binding ***protein*** , are probably important for trophoblast growth and development. Immuno-protection of the embryo at this stage may be mediated by embryo derived factors that inactivate macrophages and by a population of large, hormone dependent Lyt 2+ (CD8+) suppressor cells. It is possible that these CD8+ cells respond to progesterone and secrete molecules that inactivate natural effector (NK-type) cells against trophoblast. Prostaglandins (PGE2) may play a brief role in immunosuppression at the time of implantation but its role is probably more important with respect to the decidual response. Defects in the pre- and peri-implantation stages of pregnancy may lead to delayed failure in the form of clinical miscarriage.

L2 ANSWER 214 OF 302 MEDLINE
AN 91299812 MEDLINE
TI Identification and cellular distribution of distinct ***proteins*** forming human ***GM*** - ***CSF*** receptor.
AU Chiba S; Shibuya K; Piao Y F; Tojo A; Sasaki N; Matsuki S; Miyagawa K; Miyazono K; Takaku F
CS Department of Internal Medicine, Faculty of Medicine, University of Tokyo, Japan..
SO CELL REGULATION, (1990 Mar) 1 (4) 327-35.
Journal code: A1U. ISSN: 1044-2030.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 9110
AB Two ***proteins*** forming the receptor for human ***granulocyte*** - ***macrophage*** ***colony*** - ***stimulating*** ***factor*** (GM-CSF)1 were identified and characterized. One with apparent Mr of about 80,000 was defined as alpha-chain and has Kd of 0.7-2.8 nM. The other binding molecule with apparent Mr of about 135,000 was defined as beta-chain and is related to the high-affinity binding with Kd of 10-40 pM. The binding kinetic studies confirmed that the 125I-GM-CSF associated slower to and dissociated more rapidly from the alpha-chain than the beta-chain. The alpha-chain is expressed not only on hemopoietic cells but also on full-term placental tissues, choriocarcinoma

cells, and other solid tumor cells. In contrast, the distribution of the beta-chain is restricted on hemopoietic cells. The alpha-chain probably corresponds to the low-affinity GM-CSF receptor whose cDNA has been cloned and sequenced.

L2 ANSWER 215 OF 302 MEDLINE
AN 91288552 MEDLINE
TI Enhanced hematopoietic activity of a human ***granulocyte*** / ***macrophage*** ***colony*** - ***stimulating*** ***factor*** -interleukin 3 fusion ***protein*** .
AU Curtis B M; Williams D E; Broxmeyer H E; Dunn J; Farrah T; Jeffery E; Clevenger W; deRoos P; Martin U; Friend D; et al
CS Immunex Research and Development Corporation, Seattle, WA 98101..
NC R37 CA-36464 (NCI)
RO1 CA 36740 (NCI)
SO PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES
OF AMERICA, (1991 Jul 1) 88 (13) 5809-13.
Journal code: PV3. ISSN: 0027-8424.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
EM 9110
AB Granulocyte/macrophage colony-stimulating factor-interleukin 3 (***GM*** - ***CSF*** -IL-3) fusion ***proteins*** were generated by construction of a plasmid in which the coding regions of human GM-CSF and IL-3 cDNAs were connected by a synthetic linker sequence followed by subsequent expression in yeast. Both GM-CSF-IL-3 and IL-3- ***GM*** - ***CSF*** fusion ***proteins*** were purified to homogeneity and shown to bind to cell-surface receptors through either their GM-CSF or IL-3 domains. The fusion proteins exhibited enhanced receptor affinity, proliferative activity, and hematopoietic colony-stimulating activity compared with either IL-3 and/or GM-CSF alone. This suggests that ***GM*** - ***CSF*** -IL-3 fusion ***proteins*** may hold future promise as therapeutic agents.

L2 ANSWER 216 OF 302 MEDLINE
AN 91277428 MEDLINE
TI Augmentation of granulocyte/macrophage colony-stimulating factor expression by ultraviolet irradiation is mediated by interleukin 1 in Pam 212 keratinocytes.
AU Nozaki S; Abrams J S; Pearce M K; Sauder D N
CS Department of Dermatology, Showa University, Tokyo, Japan..
SO JOURNAL OF INVESTIGATIVE DERMATOLOGY, (1991 Jul) 97 (1) 10-4.
Journal code: IHZ. ISSN: 0022-202X.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
EM 9110
AB Keratinocytes are a potent source of a variety of cytokines including granulocyte-macrophage colony-stimulating factor (GM-CSF). In this study, we have shown that ultraviolet B (UVB) irradiation augments GM-CSF mRNA expression by murine keratinocytes. This is reflected in the increased production of ***GM*** - ***CSF*** ***protein*** by these cells. In the same cell population, exposure to UVB irradiation increases interleukin 1 alpha (IL-1 alpha) mRNA and IL-1 protein as detected by bioactivity. This increase in IL-1 alpha precedes the increase of GM-CSF mRNA. Addition of recombinant IL-1 alpha to the medium increases GM-CSF mRNA expression. Anti-IL-1 alpha antibodies can completely inhibit UV-augmented GM-CSF mRNA expression. These results demonstrate that UVB irradiation-induced augmentation of GM-CSF is mediated by UV-induced IL-1 alpha.

L2 ANSWER 217 OF 302 MEDLINE
AN 91271333 MEDLINE
TI Reconstitution of functional receptors for human ***granulocyte*** / ***macrophage*** ***colony*** - ***stimulating*** ***factor*** (***GM*** - ***CSF***): evidence that the ***protein*** encoded by the AIC2B cDNA is a subunit of the murine GM-CSF receptor.
AU Kitamura T; Hayashida K; Sakamaki K; Yokota T; Arai K; Miyajima A
CS Department of Molecular Biology, DNAX Research Institute of Molecular and Cellular Biology, Palo Alto, CA 94304..
SO PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES
OF AMERICA, (1991 Jun 15) 88 (12) 5082-6.
Journal code: PV3. ISSN: 0027-8424.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
EM 9109
AB The high-affinity receptor for human granulocyte/macrophage colony-stimulating factor (hGM-CSF) is composed of two subunits, alpha and beta. The alpha subunit binds GM-CSF with low affinity, whereas the beta subunit does not bind GM-CSF by itself. The alpha and beta subunits together form the high-affinity GM-CSF receptor. The beta subunit has extensive sequence homology with the mouse interleukin 3 (IL-3) receptor (AIC2A) and its homologue (AIC2B) that does not bind IL-3 or other cytokines including GM-CSF. To examine the function of these receptor components, we expressed the alpha subunit of the hGM-CSF receptor with the human beta subunit or the mouse AIC2A or AIC2B in a mouse IL-3-dependent pro-B-cell line, Ba/F3, and in a mouse IL-2-dependent T-cell line, CTLL2. Coexpression of the alpha and beta subunits in Ba/F3 and CTLL2 cells resulted in high-affinity hGM-CSF binding and growth response to low concentrations of hGM-CSF. Whereas Ba/F3 cells expressing the alpha subunit alone proliferated in response to high concentrations of hGM-CSF, CTLL2 cells expressing the alpha subunit alone did not respond to hGM-CSF at all. Since Ba/F3 cells express endogenous AIC2A and AIC2B whereas CTLL2 expresses neither of them, we examined the possibility that either AIC2A or AIC2B is involved in the formation of a functional GM-CSF receptor. The expression of the human alpha subunit with AIC2B, but not with AIC2A, in CTLL2 cells conferred a growth response to hGM-CSF. These results indicate that the beta subunit of the GM-CSF receptor is required for generation of growth signals and that AIC2B is likely the beta subunit of the mouse GM-CSF receptor.

L2 ANSWER 218 OF 302 MEDLINE
AN 91217640 MEDLINE
TI Activation of the adhesive capacity of CR3 on neutrophils by endotoxin: dependence on lipopolysaccharide binding protein and CD14.
AU Wright S D; Ramos R A; Hermanowski-Vosatka A; Rockwell P; Detmers P A
CS Laboratory of Cellular Physiology and Immunology, Rockefeller University, New York, New York 10021..
NC AI-22003 (NIAID)
AI-24775 (NIAID)
GM-40791 (NIGMS)
SO JOURNAL OF EXPERIMENTAL MEDICINE, (1991 May 1) 173 (5) 1281-6.
Journal code: I2V. ISSN: 0022-1007.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
EM 9108
AB Tumor necrosis factor alpha, granulocyte colony-stimulating factor, ***granulocyte*** / ***macrophage*** ***colony*** - ***stimulating*** ***factor*** , and formyl ***peptide*** were each found to cause a twofold increase in expression of CD14 on the surface of polymorphonuclear leukocytes (PMN). Upregulation of CD14 was complete by 20 min and thus appeared to result from expression of preformed stores of protein. The CD14 on the surface of PMN was shown to serve two biological functions. It bound particles coated with complexes of lipopolysaccharide (LPS) and LPS binding protein (LBP). This binding activity was enhanced by agonists that upregulated CD14 expression and may serve in the clearance of Gram-negative bacteria opsonized with LBP. Interaction of CD14 with LPS in the presence of LBP or serum also caused a dramatic, transient increase in the adhesive activity of CR3 (CD11b/CD18) on PMN. Enhanced activity of CR3 and other members of the CD11/CD18 family underlies many of the known physiological responses of PMN to LPS and may be a central feature of the in vivo responses of PMN to endotoxin.

L2 ANSWER 219 OF 302 MEDLINE
AN 91217151 MEDLINE
TI Interactions of dimethyl sulfoxide and granulocyte-macrophage colony-stimulating factor on the cell cycle kinetics and phosphoproteins of G1-enriched HL-60 cells: evidence of early effects on lamin B phosphorylation.
AU Brennan J K; Lee K S; Frazel M A; Keng P C; Young D A
CS Department of Medicine, University of Rochester School of Medicine and Dentistry, New York..

NC HL-18208 (NHLBI)
CA 11198 (NCI)
DK16177 (NIDDK)
SO JOURNAL OF CELLULAR PHYSIOLOGY, (1991 Mar) 146 (3) 425-34.
Journal code: HNB. ISSN: 0021-9541.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
EM 9108
AB We have found that GM-CSF and DMSO have antagonistic effects on the proliferation but not maturation of asynchronously growing HL-60 cells such that growth in the presence of both more closely resembles normal hematopoiesis (Brennan et al., J. Cell Physiol. 132:246, 1987). Studies were undertaken to determine whether or not the agents affected the same mitogenic pathway and locus in the cell cycle. HL-60 populations containing at least 90% G1 cells were obtained by centrifugal elutriation, exposed to 100 u/ml recombinant human GM-CSF and/or 0-1.25% DMSO, and phosphoprotein changes quantified on autoradiograms of [32P]-orthophosphate-labeled cell proteins separated by giant 2-D gel electrophoresis. Results were correlated with 1) intracellular pH, determined by measurement of BCECF fluorescence; 2) [32P]-orthophosphate uptake; 3) cell cycle progression, determined by flow quantitation of DNA content in mithramycin or propidium iodide-stained cells; and 4) growth, determined by cell volume and concentration. GM-CSF stimulated and DMSO inhibited the ***GM*** - ***CSF*** -stimulated phosphorylation of 1 ***protein*** (approximately 65 kDa, p.i. 5.6) within 2 min of exposure. These effects were sustained through G1, not associated with changes in intracellular pH, and preceded similar antagonistic effects on phosphate uptake (15-30 minutes), cell volume change (16-24 hr), and cell concentration increase (28-32 hr). GM-CSF accelerated and DMSO inhibited G1 to S transit with the most marked antagonism observed in the second cycle following synchronization (28 to 40 hrs). Cell maturation (morphology, NBT reduction) was dominated by DMSO and not antagonized by GM-CSF. We have identified p65 as the nuclear intermediate filament protein, lamin B, on the basis of its locus on gels and its binding of a monoclonal antibody to intermediate filaments and antiserum to human lamin B on immunoblots. These studies suggest that at least part of the GM-CSF-DMSO antagonism is exerted through the same mitogenic pathway, that a major locus of cytokinetic effect is on G1 to S transit, and that nuclear envelope protein phosphorylation is an important early event.

L2 ANSWER 220 OF 302 MEDLINE
AN 91208402 MEDLINE
TI Dexamethasone and 1,25-dihydroxyvitamin D3, but not cyclosporine A, inhibit production of granulocyte-macrophage colony-stimulating factor in human fibroblasts.
AU Tobler A; Marti H P; Gimmi C; Cachelin A B; Saurer S; Fey M F
CS Department of Medicine, Inselspital Berne, Switzerland..
SO BLOOD, (1991 May 1) 77 (9) 1912-8.
Journal code: A8G. ISSN: 0006-4971.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Abridged Index Medicus Journals; Priority Journals; Cancer Journals
EM 9108
AB Tumor necrosis factor alpha (TNF alpha) stimulates granulocyte-macrophage colony-stimulating factor (GM-CSF) production in human fibroblasts and other mesenchymal cells. However, relatively little is known about agents that downregulate cytokine production in these cells. In the present report we show that dexamethasone (Dexa), a synthetic glucocorticoid, markedly reduced GM-CSF production in TNF alpha-stimulated fibroblasts at both the protein and the RNA levels. CSF activity, ***GM*** - ***CSF*** ***protein*** , and RNA levels, determined by an in vitro colony-forming assay in normal human bone marrow cells, by an enzyme immunoassay, and by Northern blotting assay, were reduced to greater than 90% of control values by Dexa (1 mumol/L). Similarly, 1,25-dihydroxyvitamin D3 [1,25(OH)2D3], a hormone with possible physiologic immunoregulatory significance, reduced GM-CSF expression in a concentration- and time-dependent manner. However, this repression was less pronounced than that of Dexa, and in part due to a decreased proliferative activity. In contrast, cyclosporine A (CsA), another immunosuppressive agent, did not alter GM-CSF expression in TNF alpha-stimulated fibroblasts. Our in vitro studies suggest that by inhibiting GM-CSF production in fibroblasts, glucocorticoids and possibly 1,25(OH)2D3, but not CsA, may attenuate TNF alpha-mediated inflammatory processes and influence the regulation of hematopoiesis.

L2 ANSWER 221 OF 302 MEDLINE
AN 91203914 MEDLINE
TI Modulation of c-kit mRNA and protein by hemopoietic growth factors.
AU Welham M J; Schrader J W
CS Biomedical Research Centre, University of British Columbia, Vancouver, Canada..
SO MOLECULAR AND CELLULAR BIOLOGY, (1991 May) 11 (5) 2901-4.
Journal code: NGY. ISSN: 0270-7306.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 9107
AB We examined the effects of various hemopoietins on c-kit mRNA and ***protein*** expression. Interleukin-3 (IL-3), ***granulocyte*** - ***macrophage*** ***colony*** - ***stimulating*** ***factor*** , and erythropoietin, but not IL-4, down-regulated levels of c-kit mRNA expressed by mast cells and stem cell progenitors. The effect of IL-3 was dominant and independent of cell growth or viability and was paralleled by reduced expression in c-kit protein. These observations indicate that regulation of c-kit expression is closely interlinked with the molecular mechanisms triggered by erythropoietin, IL-3, and granulocyte-macrophage colony-stimulating factor.

L2 ANSWER 222 OF 302 MEDLINE
AN 91199046 MEDLINE
TI Hematopoietic effects of a ***granulocyte*** - ***macrophage*** ***colony*** - ***stimulating*** ***factor*** /interleukin-3 fusion ***protein*** .
AU Williams D E; Park L S
CS Immunex Research and Development Corporation, Seattle, WA 98101..
SO CANCER, (1991 May 15) 67 (10 Suppl) 2705-7. Ref: 5
Journal code: CLZ. ISSN: 0008-543X.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LA English
FS Abridged Index Medicus Journals; Priority Journals; Cancer Journals
EM 9107
AB The common functional characteristics of granulocyte-macrophage colony-stimulating factor (GM-CSF) and interleukin-3 (IL-3) may be explained by the presence of a subpopulation of cell surface receptors capable of binding both growth hormones. A ***GM*** - ***CSF*** /IL-3 fusion ***protein*** (pIXY 321) was produced in a yeast expression host. Receptor binding studies with HL-60, JM-1, AML-193, and KG-1 cell lines suggested that the GM-CSF and IL-3 regions had adopted a native conformation within the fusion protein. The fusion protein also exhibited enhanced biologic activity compared with GM-CSF or IL-3 in assays of normal, primary human hematopoietic progenitor cells. pIXY 321 may offer significant clinical advantages over the individual cytokines.

L2 ANSWER 223 OF 302 MEDLINE
AN 91192528 MEDLINE
TI Stimulation of pancreas and gastric carcinoma cell growth by interleukin 3 and granulocyte-macrophage colony-stimulating factor.
AU Dippold W G; Klingel R; Kerlin M; Schwaeble W; Meyer zum Buschenfelde K H
CS Department of Internal Medicine I, Johannes Gutenberg-Universitat Mainz, Germany..
SO GASTROENTEROLOGY, (1991 May) 100 (5 Pt 1) 1338-44.
Journal code: FH3. ISSN: 0016-5085.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Abridged Index Medicus Journals; Priority Journals; Cancer Journals
EM 9107
AB Hematopoietic growth factors have recently been well characterized by complementary DNA cloning. For human epidermal growth factor, ***granulocyte*** - ***macrophage*** ***colony*** - ***stimulating*** ***factor*** recombinant ***proteins*** have been expressed in Escherichia coli. To reduce the toxic side effects of chemotherapy on the bone marrow, recombinant human granulocyte-macrophage colony-stimulating factor and recombinant human interleukin 3 were applied to patients suffering of gastrointestinal cancers. To determine the influence of recombinant human granulocyte-macrophage colony-stimulating factor and

recombinant human interleukin 3 on human pancreas and gastric cancer cell cells in vitro, a sensitive microculture test system was established that allows precise quantification of proliferation. A more than twofold enhancement of proliferation was observed by interleukin 3 and granulocyte-macrophage colony-stimulating factor in two of two cell cultures derived from gastric carcinoma cells, while two of nine cultures from pancreas carcinoma cells have shown enhanced cell growth in the presence of recombinant human interleukin 3 or recombinant human granulocyte-macrophage colony-stimulating factor. In comparison, recombinant human epidermal growth factor increased cell growth in two of two gastric and in five of nine pancreas carcinoma cultures. In general, 1-10 ng/mL of the growth factors yielded the highest growth rate, but even 1-pg amounts produced increased cell growth. Expression of messenger RNA for granulocyte-macrophage colony-stimulating factor, interleukin 3, and the oncogene HER2/neu remained undetectable in all of the tested cell lines, while the various abundance of messenger RNA for the epidermal growth factor receptor was different in each cell line. The reported results imply that the hematopoietic growth factors interleukin 3 and granulocyte-macrophage colony-stimulating factor influence cellular growth of pancreas and gastric carcinoma cells by a paracrine mechanism and may possess a more general regulatory function than originally anticipated.

L2 ANSWER 224 OF 302 MEDLINE
AN 91170278 MEDLINE
TI Granulocyte-macrophage colony-stimulating factor induces transcriptional activation of Egr-1 in murine peritoneal macrophages.
AU Liu J W; Lacy J; Sukhatme V P; Coleman D L
CS Department of Internal Medicine, Yale University School of Medicine, West Haven, Connecticut..
SO JOURNAL OF BIOLOGICAL CHEMISTRY, (1991 Mar 25) 266 (9) 5929-33.
Journal code: HIV. ISSN: 0021-9258.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
EM 9106
AB Granulocyte-macrophage colony-stimulating factor (GM-CSF) is a pleiotropic hematopoietic growth factor that induces both growth and differentiation of tissue macrophages. The subcellular mechanism of action of GM-CSF is unknown. We have examined the effect of GM-CSF on the immediate early response gene, Egr-1, in murine peritoneal macrophages. Our data demonstrate that recombinant GM-CSF (25 units/ml) produces a 12-fold increase in Egr-1 mRNA within 30 min. Pretreatment with cycloheximide (10 micrograms/ml) had no effect on the ability of GM-CSF to increase Egr-1 mRNA. In nuclear runoff studies, GM-CSF increased the transcription rate of Egr-1 by 10-fold at 10 min. The maximal effect on Egr-1 transcription occurred at 25 min (13-fold) and decreased by 45 min. The half-life of Egr-1 mRNA in GM-CSF-treated macrophages is 13-21 min. We were unable to calculate the half-life in control cells, however, because of the short half-life and low level of constitutive expression of Egr-1 mRNA. Endogenous protein kinase C activity in macrophages was depleted by treatment with 12-O-tetradecanoylphorbol-13-acetate for 24 h. ***GM*** - ***CSF*** increased Egr-1 mRNA in ***protein*** kinase C-depleted macrophages, whereas the stimulatory effect of 12-O-tetradecanoylphorbol-13-acetate on Egr-1 was blocked. These data show that GM-CSF rapidly increases transcription of Egr-1 mRNA. The effect of GM-CSF on Egr-1 mRNA does not require de novo protein synthesis or protein kinase C. These findings provide a basis for investigating the molecular mechanism of action of GM-CSF in tissue macrophages.

L2 ANSWER 225 OF 302 MEDLINE
AN 91160276 MEDLINE
TI Role of raf-1 ***protein*** kinase in IL-3 and ***GM*** - ***CSF*** -mediated signal transduction.
AU Rapp U R; Troppmair J; Carroll M; May S
CS National Cancer Institute, Laboratory of Viral Carcinogenesis, Frederick, MD 21701..
SO CURRENT TOPICS IN MICROBIOLOGY AND IMMUNOLOGY, (1990) 166 129-39.
Journal code: DWQ. ISSN: 0070-217X.
CY GERMANY: Germany, Federal Republic of
DT Journal; Article; (JOURNAL ARTICLE)
LA English
EM 9106

L2 ANSWER 226 OF 302 MEDLINE
AN 91137799 MEDLINE
TI Identification of functionally distinct domains of human granulocyte-macrophage colony-stimulating factor using monoclonal antibodies.
AU Kanakura Y; Cannistra S A; Brown C B; Nakamura M; Seelig G F; Prosise W W; Hawkins J C; Kaushansky K; Griffin J D
CS Division of Tumor Immunology, Dana-Farber Cancer Institute, Boston, MA 02115..
NC CA36167 (NCI)
CA34183 (NCI)
SO BLOOD, (1991 Mar 1) 77 (5) 1033-43.
Journal code: A8G. ISSN: 0006-4971.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Abridged Index Medicus Journals; Priority Journals; Cancer Journals
EM 9105
AB Granulocyte-macrophage colony-stimulating factor (GM-CSF) is a glycoprotein that is required for the survival, growth, and differentiation of hematopoietic progenitor cells. Although the primary structure of GM-CSF is known from cDNA cloning, the relationship between structure and function of GM-CSF is not fully understood. Fifteen different monoclonal antibodies (MoAbs) to human GM-CSF were generated to map immunologically distinct areas of the molecule. Each of the MoAbs was biotinylated and shown by enzyme-linked immunosorbent assay to bind to recombinant GM-CSF that had been affixed to a solid phase. Each of the 15 unconjugated MoAbs was then used to compete with each biotinylated MoAb for binding to GM-CSF. These cross-blocking studies identified eight distinct epitopes of native GM-CSF. Seven of these epitopes were also present in denatured GM-CSF by Western blotting, and four of the epitopes were at least partially conserved on GM-CSF that was reduced in beta-mercaptoethanol. MoAbs to four of eight epitopes neutralized both recombinant (glycosylated and nonglycosylated) and natural human GM-CSF in a GM colony-forming unit (CFU-GM) assay and blocked GM-CSF-induced activation of neutrophils. For most of the antibodies there was a good correlation between neutralizing activity and the capacity to block binding of 125I-GM-CSF to neutrophils or blasts. Non-neutralizing antibodies to one epitope partially blocked binding of 125I-GM-CSF to neutrophils. None of the MoAbs neutralized interleukin-3, G-CSF, or M-CSF. The locations of seven of the epitopes could be partially mapped with regard to the amino acid structure by determining reactivity to ***GM*** - ***CSF*** synthetic ***peptides*** or to human-mouse chimeric GM-CSFs. The neutralizing antibodies were found to map to amino acids 40-77, 78-94, or 110-127. Thus, these MoAbs are useful to identify functional domains of GM-CSF and in identifying regions that are likely to be involved in receptor interaction.

L2 ANSWER 227 OF 302 MEDLINE
AN 91105617 MEDLINE
TI A double-blind placebo-controlled study with granulocyte-macrophage colony-stimulating factor during chemotherapy for ovarian carcinoma.
AU de Vries E G; Biesma B; Willemse P H; Mulder N H; Stern A C; Aalders J G; Vellenga E
CS Department of Internal Medicine, University Hospital Groningen, The Netherlands..
SO CANCER RESEARCH, (1991 Jan 1) 51 (1) 116-22.
Journal code: CNF. ISSN: 0008-5472.
CY United States
DT (CLINICAL TRIAL)
(CONTROLLED CLINICAL TRIAL)
Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
EM 9105
AB In a placebo-controlled double-blind dose-finding trial, 15 patients with ovarian cancer stage III or IV received daily s.c. 1.5, 3, or 6 micrograms/kg recombinant human granulocyte-macrophage colony-stimulating factor (GM-CSF). At each dose step three patients received recombinant human GM-CSF, and two received placebo. Chemotherapy comprised 6 cycles of carboplatin, 300 mg/m2, and cyclophosphamide, 750 mg/m2, by i.v. bolus on day 1 every 4 weeks. GM-CSF, given on days 6-12 on an outpatient basis, raised the mean leukocyte count on days 7, 10, and 15 and the mean neutrophil count on days 7 and 10 at all dose levels as compared with the control group. Neutrophil counts of less than 0.5 x 10(9)/liter occurred in 20 of 22 cycles in the control group and in 5 of 17 cycles at the 6-micrograms/kg/day GM-CSF dose level (P less than 0.0005). In comparison with the control group, the mean eosinophil count was

higher on days 10 and 15 at all GM-CSF doses, as was the mean monocyte count on day 15. The mean platelet count was raised at the 3- and 6-micrograms GM-CSF doses on days 15 and 22. Chemotherapy dose reduction or postponement due to myelotoxicity occurred in 9 of 28 cycles in the placebo groups versus 5 of 44 cycles in the GM-CSF group (not significant). Local skin infiltrates at the GM-CSF injection sites occurred in 8/9 patients, leading to premature removal of two patients from the study. Capillary leakage of 131I-albumin was increased in all patients 5 days after the first chemotherapy course but was not significantly affected by 4 days of GM-CSF treatment. Tumor necrosis factor alpha and C-reactive ***protein*** serum levels increased during ***GM*

=> d l2 275-302 bib ab

L2 ANSWER 275 OF 302 MEDLINE
AN 88285848 MEDLINE
TI Keratinocyte derived T-cell growth factor (KTGF) is identical to granulocyte macrophage colony stimulating factor (GM-CSF).
AU Kupper T S; Lee F; Coleman D; Chodakewitz J; Flood P; Horowitz M
CS Department of Dermatology, Yale University School of Medicine, New Haven, Connecticut..
NC AI 25082-01
SO JOURNAL OF INVESTIGATIVE DERMATOLOGY, (1988 Aug) 91 (2) 185-8.
Journal code: IHZ. ISSN: 0022-202X.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
EM 8811
AB Keratinocyte derived T-cell growth factor was initially described as a product of cultured neonatal keratinocytes and keratinocyte cell lines that induced the proliferation of HT-2 cells, a murine T-cell line that responds to IL-2 and IL-4 by incorporating 3H-Thymidine. Subsequently, KTGF has been purified to high specific activity and found to be distinct from IL-2 and IL-4 by a variety of biochemical, immunologic, and immunochemical criteria. Because it was found that certain HT-2 cell lines also proliferated in response to GM-CSF, the present study asked whether KTGF was related to GM-CSF. In this study, we demonstrate that antibodies to recombinant murine GM-CSF completely neutralize the capacity of KTGF to induce HT-2 proliferation without interfering with IL-2 or IL-4 induced HT-2 proliferation. Furthermore, poly-A+ RNA homologous to murine GM-CSF cDNA as judged by S1 nuclease analysis was detected in Pam 212 cells, and ***protein*** serologically homologous to ***GM*** - ***CSF*** was found in Pam 212 conditioned medium. We conclude that KTGF is identical to GM-CSF. The T-cell activating properties of GM-CSF require further exploration.

L2 ANSWER 276 OF 302 MEDLINE
AN 88285689 MEDLINE
TI Structure-function studies of human granulocyte-macrophage colony-stimulating factor. Identification of residues required for activity.
AU Clark-Lewis I; Lopez A F; To L B; Vadas M A; Schrader J W; Hood L E; Kent S B
CS California Institute of Technology, Division of Biology, Pasadena..
SO JOURNAL OF IMMUNOLOGY, (1988 Aug 1) 141 (3) 881-9.
Journal code: IFB. ISSN: 0022-1767.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Abridged Index Medicus Journals; Priority Journals; Cancer Journals
EM 8811
AB Human ***granulocyte*** - ***macrophage*** ***colony*** ***stimulating*** ***factor*** (hGM CSF), a ***protein*** containing 127 amino acids, was chemically synthesized by using automated stepwise solid-phase methods. The unpurified synthetic hGM-CSF had the same range of actions on hemopoietic cells as the purified recombinant protein. The structural requirements for the activities of synthetic hGM-CSF were examined by the design and synthesis of fragments and analogs. The synthetic fragment, hGM-CSF (54-127), containing all four of the cysteine residues found in the intact protein, lacked detectable activity. Assays of fragments shortened at the N terminus showed that the residues 1-13 were not required for activity, but that the integrity of residues 14-25, particularly residues 16, 17, and 18, was critical for biologic activity. The 14-25 region is predicted to form the first alpha-helix in hGM-CSF. Synthetic peptides within the N-terminal 53 residue region lacked detectable activity. The synthetic analog hGM-CSF (1-121), which lacks the C-terminal 6 residues, had similar activity to hGM-CSF (1-127) indicating that residues 122-127 are not required for activity. An analog, [Ala88] hGM-CSF (14-96), which lacks the hydrophobic C-terminal region and 2 cysteine residues, had low but readily detectable activity suggesting that residues 14-96 are sufficient for detectable synthetic hGM-CSF activity, although the presence of residues 97-121 are required for full activity. No dissociation of the multiple biological activities of hGM-CSF was detected.

L2 ANSWER 277 OF 302 MEDLINE
AN 88257449 MEDLINE
TI 1,25-Dihydroxyvitamin D3 modulates the expression of a lymphokine (granulocyte-macrophage colony-stimulating factor) posttranscriptionally.
AU Tobler A; Miller C W; Norman A W; Koeffler H P
CS Department of Medicine, University of California, Los Angeles 90024..
NC CA-26038
CA-32737
CA-33936
+
SO JOURNAL OF CLINICAL INVESTIGATION, (1988 Jun) 81 (6) 1819-23.
Journal code: HS7. ISSN: 0021-9738.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Abridged Index Medicus Journals; Priority Journals; Cancer Journals
EM 8810
AB We recently showed that 1,25(OH)2D3 sensitively inhibited the expression of granulocyte-macrophage colony-stimulating factor (GM-CSF) in normal human mitogen-activated peripheral blood lymphocytes and in the human T lymphotropic virus I immortalized T cell line known as S-LB1 at the levels of both mRNA and protein. Using S-LB1 cells as a model system the present paper identifies at least in part the mechanisms by which 1,25(OH)2D3 regulates the expression of GM-CSF. Time-course studies demonstrated that by 6 and 48 h of exposure of S-LB1 cells to 1,25(OH)2D3 (10(-8) M) the GM-CSF mRNA levels were reduced by 50 and 90%, respectively. Studies using cycloheximide as a protein synthesis inhibitor showed that the inhibitory action of 1,25(OH)2D3 on ***GM*** - ***CSF*** expression was dependent on new ***protein*** synthesis. In vitro nuclear run-on assays demonstrated that 1,25(OH)2D3 (10(-8) M) did not change the rate of transcription of the GM-CSF gene. The t1/2 of GM-CSF mRNA, however, was profoundly reduced by 1,25(OH)2D3 when transcription was blocked by actinomycin D compared with the half-life of GM-CSF in the presence of actinomycin D alone (t1/2, less than 0.5 and 4 h, respectively). Taken together, these results demonstrate that 1,25(OH)2D3 regulates expression of the lymphokine GM-CSF posttranscriptionally by influencing the stability of GM-CSF mRNA.

L2 ANSWER 278 OF 302 MEDLINE
AN 88229741 MEDLINE
TI A sensitive, rapid assay for the detection of human granulocyte-macrophage colony stimulating factor.
AU Conlon P J; McMasters D; Prickett K S
CS Immunex Corporation, Seattle, WA 98101..
SO JOURNAL OF BIOLOGICAL RESPONSE MODIFIERS, (1987 Dec) 6 (6) 637-46.
Journal code: JBM. ISSN: 0732-6580.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 8809
AB Several monoclonal antibodies were developed against recombinant human granulocyte colony stimulating factor (hu- ***GM*** - ***CSF***). All were reactive to the ***protein*** by enzyme linked immunoabsorbent assay (ELISA), and one, 1G2 was capable of immunoprecipitating significant levels of radiolabeled hu-GM-CSF. When 1G2 and a second GM-CSF reactive monoclonal antibody, 3G11, were used in a double determinant assay, the level of detection of hu-GM-CSF in solution was approximately 500 ng/ml. Additional sensitivity was gained by using affinity purified rabbit polyclonal antibodies, together with the monoclonal 1G2. Using such a configuration in a double determinant assay one could detect 10-90 ng/ml of human-GM-CSF in solution with no reactivity observed to CSF-1 or granulocyte-CSF.

L2 ANSWER 279 OF 302 MEDLINE

AN 88217297 MEDLINE
TI Myeloperoxidase and oncogene expression in GM-CSF induced bone marrow differentiation.
AU Jaffe B D; Sabath D E; Johnson G D; Moscinski L C; Johnson K R; Rovera G; Nauseef W M; Prystowsky M B
CS Department of Pathology, University of Pennsylvania School of Medicine, Philadelphia..
NC AI-21681
5-T32-GM-07170
CA-09140
SO ONCOGENE, (1988 Feb) 2 (2) 167-74.
Journal code: ONC. ISSN: 0950-9232.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
EM 8808
AB DNA synthesis, morphology, specific RNA accumulation and rates of specific ***protein*** synthesis in ***GM*** - ***CSF*** stimulated bone marrow progenitor cells were studied. DNA synthesis increased markedly for 64 hours and then gradually decreased to 5% maximal activity by 160 hours. Morphologic examination 40 to 64 hours after stimulation revealed an increasing proportion of immature myeloid cells. After this proliferative peak, cells differentiated into segmented neutrophils and monocytes/macrophages; only mature forms were present by 160 hours. Accumulation of mRNA for c-myb and c-myc was maximal at 40 hours just prior to maximal [3H]thymidine incorporation, while maximal accumulation of histone type 3 (H3) was coincident with maximal [3H]thymidine incorporation at 64 hours. As proliferation decreased and differentiation proceeded, levels of mRNA for c-myb and H3 decreased markedly, while levels of RNA for c-myc decreased gradually and remained elevated above day 0 levels. Levels of c-fos mRNA fluctuated slightly during the first 64 hours of culture and increased 13-fold by 160 hours when mature cells were present. Similarly, beta-2 microglobulin mRNA increased steadily to maximal levels at 112 to 160 hours which were 15-fold higher than day 0 levels. Myeloperoxidase (MPO) mRNA was present in maximal amounts at 40 to 64 hours after stimulation with GM-CSF as the number of immature myeloid cells peaked. Immunoprecipitation of MPO from pulse-labeled cell lysates demonstrated a 7-fold rise in synthetic rate of MPO of 64 hours and a 28-fold decline by 160 hours when only 5% immature myeloid cells were present. Thus, MPO protein synthesis closely follows MPO mRNA accumulation. Immunoprecipitation of lactoferrin, a marker of myeloid secondary granules, demonstrated a gradual 5-fold increase in synthetic rate as the cells matured. Taken together, these data show that maximal expression of the early myeloid differentiation enzyme myeloperoxidase in GM-CSF stimulated normal bone marrow cells occurs during peak proliferation of immature myeloid cells.

L2 ANSWER 280 OF 302 MEDLINE
AN 88187598 MEDLINE
TI Leukotriene production in human neutrophils primed by recombinant human granulocyte/macrophage colony-stimulating factor and stimulated with the complement component C5A and FMLP as second signals.
AU Dahinden C A; Zingg J; Maly F E; de Weck A L
CS Institute of Clinical Immunology, Inselspital, Bern, Switzerland..
SO JOURNAL OF EXPERIMENTAL MEDICINE, (1988 Apr 1) 167 (4) 1281-95.
Journal code: I2V. ISSN: 0022-1007.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
EM 8807
AB Neutrophils (PMN) preincubated with recombinant human granulocyte/macrophage colony-stimulating factor (rhGM-CSF) for 2 h and then stimulated with the chemotactic factors, C5a or FMLP, produce substantial amounts of the lipoxygenase products 5-Hete, LTB4, and omega-oxidised LTB4 metabolites (4.36 +/- 0.95 (SEM) pM (n = 21) LTB4 and LTB4 metabolites/10(6) PMN). No lipoxygenase metabolites are detected by HPLC and RIA if purified PMN are stimulated by either GM-CSF or chemotactic factors in the absence of exogenous arachidonate. The priming effect of GM-CSF upon chemotactic factor induced generation of lipid mediators is a relatively slow process, clearly evident after 1 h and optimal after 2 h. Leukotriene generation is measurable with 0.8 U GM-CSF/10(6) PMN and is maximal with 80 U (10(-11)-10(-9) M). Upon activation of primed PMN with chemotactic factors, leukotriene synthesis is induced very rapidly. Already 2.5 min after activation the major lipoxygenase metabolites present are 20-OH LTB4 and 20-COOH LTB4. Our study shows that the synthesis of lipoxygenase metabolites from endogeneous AA can be initiated in PMN through receptor mediated processes by the appropriately timed combination of biological soluble inflammatory mediator ***peptides*** . Furthermore, these results indicate that ***GM*** - ***CSF*** not only enhances effector cell functions but can qualitatively change the mediator profile formed after activation with a second triggering signal. Such a mechanism might be important in amplifying inflammatory responses. Alternatively, lipid mediators formed might also have an intracellular or autocoid role and be responsible for the enhancement of other PMN functions like oxygen radical release.

L2 ANSWER 281 OF 302 MEDLINE
AN 88187380 MEDLINE
TI Stimulation of guanylate cyclase activity and reduction of adenylate cyclase activity by granulocyte-macrophage colony-stimulating factor in human blood neutrophils.
AU Coffey R G; Davis J S; Djeu J Y
CS Department of Pharmacology, University of South Florida, College of Medicine, Tampa 33612..
NC NC1-CM-57717-15
HD22248
SO JOURNAL OF IMMUNOLOGY, (1988 Apr 15) 140 (8) 2695-701.
Journal code: IFB. ISSN: 0022-1767.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Abridged Index Medicus Journals; Priority Journals; Cancer Journals
EM 8807
AB Human neutrophils were incubated with granulocyte-macrophage (GM)-CSF and examined for changes in second messenger systems. Twofold increases in cGMP but not cAMP were measured after 5 to 20 min with 100 U/ml GM-CSF. Guanylate cyclase activities in membrane and cytosol fractions were increased to the same extent whether measured in the presence of Mg2+ or Mn2+, or in the cytosol with Mg2+ + N-methyl-N'-nitro-N-nitroso-guanidine. Kinetic studies of the cytosol enzyme showed no changes in the Km values for Mg2+ and Mn2+dependent guanylate cyclase activities (0.91 and 0.022 mM, respectively), whereas Vm values were increased after treating intact cells with GM-CSF. Two peaks of guanylate cyclase activity were observed, one at 10 and another at 60 min after adding 100 U/ml GM-CSF, whereas only one peak at 5 min occurred with 1 U/ml. Adenylate cyclase activity was reduced by nearly 50% after adding 100 U/ml GM-CSF for 10 to 30 min. These effects were also seen in the presence of several hormonal and nonhormonal adenylate cyclase stimulators. In contrast, small increases in adenylate cyclase activity occurred after adding 1 U/ml GM-CSF. In experiments to examine the pathway of guanylate cyclase activation by GM-CSF, we observed no changes in inositol phosphates, intracellular calcium ion, or cytosolic protein kinase C. The augmentation of chemotactic ***peptide*** -induced superoxide production by ***GM*** - ***CSF*** concentrations, may be related to the effects of the higher levels of GM-CSF to stimulate late increases in guanylate cyclase or decreases in adenylate cyclase.

L2 ANSWER 282 OF 302 MEDLINE
AN 88186276 MEDLINE
TI Target-cell specificity of hematopoietic regulatory proteins for different clones of myeloid leukemic cells: two regulators secreted by Krebs carcinoma cells.
AU Shabo Y; Lotem J; Sachs L
CS Department of Genetics, Weizmann Institute of Science, Rehovot, Israel..
SO INTERNATIONAL JOURNAL OF CANCER, (1988 Apr 15) 41 (4) 622-8.
Journal code: GQU. ISSN: 0020-7136.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
EM 8807
AB The normal myeloid hematopoietic regulatory proteins include one class of proteins that induces viability and multiplication of normal myeloid precursor cells to form colonies (called MGI-1 = CSF or IL-3) and another class (called MGI-2 = DF) that induces differentiation of normal myeloid precursors without inducing cell multiplication. Different clones of myeloid leukemia cells can differ in their response to these regulatory proteins. The present experiments characterize proteins secreted by Krebs ascites carcinoma cells that induce differentiation of 2 different types of myeloid leukemic cell clones (clones II and 7-M12). The results

indicate the following: (1) Krebs cells produce 2 distinct and separable proteins, each inducing differentiation in one of the leukemic clones. (2) One protein induced differentiation of clone-II myeloid leukemic cells and of normal myeloid precursor cells was free of any colony-inducing (MGI-1 = CSF or IL-3) activity, bound to double-stranded mammalian DNA, and was thus a differentiation-inducing protein MGI-2. This MGI-2 protein (MGI-2A) was purified to a single silver-stained band on an SDS polyacrylamide gel. (3) The other protein induced differentiation of clone 7-M12 myeloid leukemic cells, did not bind to double-stranded DNA and could not be separated from the myeloid growth-inducing ***protein*** MGI-1GM (***GM*** - ***CSF***) after 6 steps of purification including high-pressure liquid chromatography. The use of specific antisera confirmed that the protein which induced differentiation of clone 7-M12 leukemic cells was MGI-1 GM. The results show that Krebs ascites tumor cells produce 2 different myeloid hematopoietic regulatory proteins that differ in their target specificity for different clones of myeloid leukemic cells.

L2 ANSWER 283 OF 302 MEDLINE
AN 88183231 MEDLINE
TI Identification of a signal-transduction pathway shared by haematopoietic growth factors with diverse biological specificity.
AU Evans S W; Rennick D; Farrar W L
CS Laboratory of Molecular Immunoregulation, National Cancer Institute, Frederick Cancer Research Facility, MD 21701-1013..
SO BIOCHEMICAL JOURNAL, (1987 Jun 15) 244 (3) 683-91.
Journal code: 9YO. ISSN: 0264-6021.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
EM 8807
AB The haematopoietic growth factors multi-colony-stimulating factor, granulocyte/macrophage colony-stimulating factor, granulocyte colony-stimulating factor and interleukin 2 specifically control the production and proliferation of distinct leucocyte series. Each growth factor acts on a unique surface receptor associated with an appropriate signal-transduction apparatus. In this report we identify a 68 kDa substrate which is phosphorylated after stimulation of different cell types with multi-colony-stimulating factor, granulocyte colony-stimulating factor and interleukin 2. The 68 kDa substrate is also phosphorylated in each cell line stimulated with synthetic diacylglycerol, a direct activator of ***protein*** kinase C. Interestingly, ***granulocyte*** / ***macrophage*** ***colony*** - ***stimulating*** ***factor*** does not induce phosphorylation of the 68 kDa molecule. The 68 kDa molecule that is phosphorylated after stimulation with each ligand yielded similar peptide maps after chymotryptic digestion; furthermore, the substrate was always phosphorylated on threonine residues. Phosphorylation of the same residues in the 68 kDa substrate suggests that activation of protein kinase C is one common signal-transduction event associated with the action of multi-colony-stimulating factor, granulocyte colony-stimulating factor and interleukin 2.

L2 ANSWER 284 OF 302 MEDLINE
AN 88124904 MEDLINE
TI Nuclear proteins interacting with the promoter region of the human granulocyte/macrophage colony-stimulating factor gene.
AU Shannon M F; Gamble J R; Vadas M A
CS Division of Human Immunology, Institute of Medical and Veterinary Science, Adelaide, South Australia..
NC CA 45822-01
SO PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES
OF AMERICA, (1988 Feb) 85 (3) 674-8.
Journal code: PV3. ISSN: 0027-8424.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
EM 8805
AB The gene for human granulocyte/macrophage colony-stimulating factor (GM-CSF) is expressed in a tissue-specific as well as an activation-dependent manner. The interaction of nuclear proteins with the promoter region of the GM-CSF gene that is likely to be responsible for this pattern of GM-CSF expression was investigated. We show that nuclear proteins interact with DNA fragments from the GM-CSF promoter in a cell-specific manner. A region spanning two cytokine-specific sequences, cytokine 1 (CK-1, 5' GAGATTCCAC 3') and cytokine 2 (CK-2, 5' TCAGGTA 3') bound two nuclear proteins [nuclear factor (NF)-GMa and NF-GMb] from GM-CSF-expressing cells in gel retardation assays. NF-GMb was inducible with phorbol 12-myristate 13-acetate and accompanied induction of GM-CSF message. NF-GMb was absent in cell lines not producing GM-CSF, some of which had other distinct binding proteins. NF-GMa and NF-GMb eluted from a heparin-Sepharose column at 0.3 and 0.6 M KCl, respectively. We hypothesize that the sequences CK-1 and CK-2 bind specific ***proteins*** and regulate ***GM*** - ***CSF*** transcription.

L2 ANSWER 285 OF 302 MEDLINE
AN 88108147 MEDLINE
TI In vivo control of differentiation of myeloid leukemic cells by recombinant granulocyte-macrophage colony-stimulating factor and interleukin 3.
AU Lotem J; Sachs L
CS Department of Genetics, Weizmann Institute of Science, Rehovot, Israel..
SO BLOOD, (1988 Feb) 71 (2) 375-82.
Journal code: A8G. ISSN: 0006-4971.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Abridged Index Medicus Journals; Priority Journals; Cancer Journals
EM 8805
AB The normal myeloid hematopoietic regulatory proteins include one class of proteins that induces viability and multiplication of normal myeloid precursor cells to form colonies (colony-stimulating factors [CSF] and interleukin 3 [IL-3], macrophage and granulocyte inducing proteins, type 7 [MGI-1]) and another class (called MGI-2) that induces differentiation of normal myeloid precursors without inducing cell multiplication. Different clones of myeloid leukemic cells can differ in their response to these regulatory proteins. One type of leukemic clone can be differentiated in vitro to mature cells by incubating with the growth-inducing ***proteins*** granulocyte-macrophage (***GM***) ***CSF*** or IL-3, and another type of clone can be differentiated in vitro to mature cells by the differentiation-inducing protein MGI-2. We have now studied the ability of different myeloid regulatory proteins to induce the in vivo differentiation of these different types of mouse myeloid leukemic clones in normal and cyclophosphamide-treated mice. The results show that in both types of mice (a) the in vitro GM-CSF- and IL-3-sensitive leukemic cells were induced to differentiate to mature cells in vivo in mice injected with pure recombinant GM-CSF and IL-3 but not with G-CSF, M-CSF, or MGI-2; (b) the in vitro MGI-2-sensitive leukemic cells differentiated in vivo by injection of MGI-2 and also, presumably indirectly, by GM-CSF and IL-3 but not by M-CSF or G-CSF; (c) in vivo induced differentiation of the leukemic cells was associated with a 20- to 60-fold decrease in the number of blast cells; and (d) all the injected myeloid regulatory proteins stimulated the normal myelopoietic system. Different normal myeloid regulatory proteins can thus induce in vivo terminal differentiation of leukemic cells, and it is suggested that these proteins can have a therapeutic potential for myeloid leukemia in addition to their therapeutic potential in stimulating normal hematopoiesis.

L2 ANSWER 286 OF 302 MEDLINE
AN 88058429 MEDLINE
TI Constitutive expression of the granulocyte-macrophage colony-stimulating factor gene in human solid tumors.
AU Mano H; Nishida J; Usuki K; Maru Y; Kobayashi Y; Hirai H; Okabe T; Urabe A; Takaku F
CS Third Department of Internal Medicine, Faculty of Medicine, University of Tokyo..
SO JAPANESE JOURNAL OF CANCER RESEARCH, (1987 Oct) 78 (10) 1041-3.
Journal code: HBA. ISSN: 0910-5050.
CY Japan
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
EM 8803
AB We detected constitutive expression of the granulocyte-macrophage colony-stimulating factor (GM-CSF) gene in 3 human solid tumors by Northern blot analysis. Two of them were also found to secrete the ***GM*** - ***CSF*** ***protein*** by colony forming unit-culture assay. Southern blot analysis of each tumor DNA showed no gross rearrangement of the GM-CSF gene. This is the first report that demonstrates expression of the GM-CSF gene in solid tumors at

the mRNA level.

L2 ANSWER 287 OF 302 MEDLINE
AN 88031809 MEDLINE
TI Regulation of cell-surface receptors for hematopoietic differentiation-inducing protein MGI-2 on normal and leukemic myeloid cells.
AU Lotem J; Sachs L
CS Department of Genetics, Weizmann Institute of Science, Rehovot, Israel..
SO INTERNATIONAL JOURNAL OF CANCER, (1987 Oct 15) 40 (4) 532-9. Journal code: GQU. ISSN: 0020-7136.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
EM 8802
AB The normal myeloid hematopoietic regulatory proteins include 4 different growth-inducing ***proteins*** (IL-3, MGI-1GM = ***GM*** - ***CSF*** , MGI-1G = G-CSF, and MGI-1M = M-CSF = CSF-1). There is also another type of normal myeloid regulatory protein (MGI-2) with no MGI-1 (CSF or IL-3) activity, which can induce differentiation of normal myeloid precursors and certain clones of myeloid leukemic cells. Studies on the binding of MGI-2 to differentiation-competent (D+) and differentiation-defective (D-) clones of mouse myeloid leukemic cells and to normal cells indicate that: (1) D+ clones of myeloid leukemic cells had about 2,500 high-affinity surface receptors per cell, like mature normal myeloid cells, and the bound MGI-2 was rapidly internalized with its cell-surface receptors at 37 degrees C causing down-regulation of MGI-2 receptors in both the normal and leukemic cells; (2) in some D- clones, the number and internalization of MGI-2 receptors were similar to those of D+ clones whereas other D- clones had only 0-100 MGI-2 receptors per cell; (3) normal thymus and lymph-node lymphocytes and T lymphoma cells did not show detectable MGI-2 receptors; (4) there was an independent expression of receptors for MGI-2 and for the 4 myeloid growth-inducing proteins on different clones of myeloid leukemic cells; and (5) none of the 4 myeloid growth-inducing proteins IL-3, MGI-1GM, MGI-1G, or MGI-1M, inhibited binding of MGI-2 to its receptors. The cytotoxic proteins lymphotoxin and tumor necrosis factor did not induce differentiation of the mouse myeloid leukemic cells and also did not inhibit binding of MGI-2 to its receptors. These results show that the myeloid differentiation-inducing protein MGI-2 binds to cell-surface receptors that are different from the receptors for the 4 myeloid growth-inducing proteins and these cytotoxic proteins.

L2 ANSWER 288 OF 302 MEDLINE
AN 87246072 MEDLINE
TI Expression and purification of native human granulocyte-macrophage colony-stimulating factor from an Escherichia coli secretion vector.
AU Libby R T; Braedt G; Kronheim S R; March C J; Urdal D L; Chiaverotti T A; Tushinski R J; Mochizuki D Y; Hopp T P; Cosman D
SO DNA, (1987 Jun) 6 (3) 221-9. Journal code: EAW. ISSN: 0198-0238.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 8710
AB The human granulocyte-macrophage colony stimulating factor (GM-CSF) was expressed and purified from a high-level Escherichia coli secretion vector. A cDNA fragment encoding mature GM-CSF was fused with the aid of a synthetic oligonucleotide to the E. coli outer membrane signal peptide (ompA) of the secretion expression vector pIN-III-ompA3. The primary construction, designated pLB5001, is under transcriptional control of the tandem lipoprotein promoter (lppP) lactose promoter-operator (lacPO), and is regulated by the lactose repressor. Upon induction, a polypeptide of MW = 14,600 was produced which had GM-CSF activity in a human bone marrow colony assay. The linker sequence between the ompA signal peptide and the amino terminus of the mature GM-CSF was removed by oligonucleotide-directed site-specific mutagenesis to produce GM-CSF with an authentic amino terminus. The resulting construct, designated pLB5001-4, expressed authentic GM-CSF with a specific activity similar to that observed for the pLB5001 specified GM-CSF. Both versions of GM-CSF were associated with the membrane fraction after osmotic shock, and were purified to homogeneity by DEAE-Sephacel chromatography, followed by reversed-phase HPLC. Amino acid sequencing from the amino terminus of the purified ***GM*** - ***CSF*** established that the ompA signal ***peptide*** was cleaved at its normal processing site in both cases.

L2 ANSWER 289 OF 302 MEDLINE
AN 87109317 MEDLINE
TI Signal recognition particle arrests elongation of nascent secretory and membrane proteins at multiple sites in a transient manner.
AU Lipp J; Dobberstein B; Haeuptle M T
SO JOURNAL OF BIOLOGICAL CHEMISTRY, (1987 Feb 5) 262 (4) 1680-4. Journal code: HIV. ISSN: 0021-9258.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
EM 8705
AB The signal recognition particle (SRP) has been shown to target nascent secretory and membrane proteins to the endoplasmic reticulum. In the wheat germ cell-free system, SRP arrests the elongation of the nascent chains until the translational complex is docked to the endoplasmic reticulum membrane where the interaction between SRP and docking protein causes a release of the nascent chain arrest. For two secretory proteins, arrested peptides of 70 amino acids have been identified (Walter, P., Ibrahimi, I., and Blobel, G. (1981) J. Cell Biol. 91, 545-550; Meyer, D. I., Krause, E., and Dobberstein, B. (1982) Nature 297, 647-650). By using an in vitro coupled transcription-translation system, we have analyzed SRP arrest and the resulting peptides of the two secretory ***proteins*** lysozyme and ***granulocyte*** - ***macrophage*** ***colony*** - ***stimulating*** ***factor*** and the membrane ***protein*** invariant chain. SRP arrested the elongation of all three proteins at multiple sites, giving rise to ladders of arrested peptides. The size of the arrested peptides increased with the time of translation, resulting in mostly full-length pre-peptides after about 40 min. This suggests that SRP arrest in transient rather than stable. Upon addition of microsomes, the SRP arrest was released, and all the blocked peptides could be chased into mature proteins or full-length precursors.

L2 ANSWER 290 OF 302 MEDLINE
AN 87076983 MEDLINE
TI Purification and properties of bacterially synthesized human granulocyte-macrophage colony stimulating factor.
AU Burgess A W; Begley C G; Johnson G R; Lopez A F; Williamson D J; Mermod J J; Simpson R J; Schmitz A; DeLamarter J F
NC CA-22556
CA-25972
AI-21876
SO BLOOD, (1987 Jan) 69 (1) 43-51. Journal code: A8G. ISSN: 0006-4971.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Abridged Index Medicus Journals; Priority Journals; Cancer Journals
EM 8704
AB Human granulocyte-macrophage colony stimulating factor (GM-CSF) has been synthesized in high yield using a temperature inducible plasmid in Escherichia coli. The human GM-CSF is readily isolated from the bacterial proteins because of its differential solubility and chromatographic properties. The bacterially synthesized form of the human GM-CSF contains an extra methionine residue at position 1, but otherwise it is identical to the polypeptide predicted from the cDNA sequence. The specific activity of 2.9 X 10(7) units/mg of ***protein*** for purified bacterially synthesized human ***GM*** - ***CSF*** indicates that despite the lack of glycosylation, the molecule is substantially in its native conformation. This molecule stimulated the same number and type of both seven- and 14-day human bone marrow colonies as the CSF alpha preparation from human placental conditioned medium. Human GM-CSF had no activity on murine bone marrow or murine leukemic cells. There was no detectable, direct stimulation of adult human erythroid burst forming units (BFU-E) by the bacterially synthesized human GM-CSF. Although impure preparations containing native human GM-CSF (eg, human placental conditioned medium) stimulated the formation of mixed colonies, even in the presence of erythropoietin, the bacterially synthesized human GM-CSF failed to stimulate the formation of mixed colonies from adult human bone marrow cells. The bacterially synthesized human GM-CSF increased N-formyl-methionyl-leucyl-phenylalanine (FMLP)-induced superoxide production and lysozyme secretion. Antibody-dependent cytotoxicity and phagocytosis by human neutrophils was stimulated by the bacterially synthesized human GM-CSF and eosinophils were also activated in the

antibody-dependent cytotoxicity assay.

L2 ANSWER 291 OF 302 MEDLINE
AN 86311343 MEDLINE
TI Recombinant human TNF induces production of granulocyte-monocyte colony-stimulating factor.
AU Munker R; Gasson J; Ogawa M; Koeffler H P
SO NATURE, (1986 Sep 4-10) 323 (6083) 79-82.
Journal code: NSC. ISSN: 0028-0836.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
EM 8612
AB Tumor necrosis factor (TNF) is synthesized by macrophages exposed to endotoxin. It produces haemorrhagic necrosis of a variety of tumours in mice and is cytostatic or cytocidal against various transformed cell lines in vitro, but viability of normal human or rodent cells is unaffected. The role of TNF is unlikely to be restricted to the rejection of tumours. Colony-stimulating factors (CSFs) are required for survival, proliferation and differentiation of haematopoietic progenitor cells. The haematopoietic growth factor known as granulocyte-monocyte colony-stimulating factor (GM-CSF) has the ability to stimulate proliferation and differentiation of normal granulocyte-monocyte and eosinophil stem cells and enhance the proliferation of pluripotent, megakaryocyte and erythroid stem cells. In addition, GM-CSF stimulates a variety of functional activities in mature granulocytes and macrophages, for example inhibition of migration, phagocytosis of microbes, oxidative metabolism, and antibody-dependent cytotoxic killing of tumour cells. We show here that TNF markedly stimulates production of ***GM*** - ***CSF*** messenger RNA and ***protein*** in normal human lung fibroblasts and vascular endothelial cells, and in cells of several malignant tissues.

L2 ANSWER 292 OF 302 MEDLINE
AN 86205971 MEDLINE
TI Structural homologies among the hemopoietins.
AU Schrader J W; Ziltener H J; Leslie K B
NC R01 CA38684-01
SO PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES
OF AMERICA, (1986 Apr) 83 (8) 2458-62.
Journal code: PV3. ISSN: 0027-8424.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
EM 8608
AB A group of cytokines characterized by a common set of target cells--namely, the pluripotential hemopoietic stem cells or their cellular derivatives--share similarities in the amino acid sequence at their N terminus or in the putative signal peptide immediately prior to the published N terminus. Murine P-cell-stimulating factor (PSF), murine and human interleukin 2 (IL-2), murine and human granulocyte-macrophage colony-stimulating factor (GM-CSF), human erythropoietin, and human interleukin 1 beta all share alanine as the N-terminal amino acid and have some similarities in the succeeding three or four amino acids. In the case of murine PSF and GM-CSF, the six N-terminal amino acids are readily cleaved from mature molecules and are lacking from the N-terminal amino acid sequences reported initially. A sixth cytokine, colony-stimulating factor 1, has an alanine followed by a similar pattern of five amino acids at the end of the putative signal ***peptide*** . ***GM*** - ***CSF*** and IL-2 have more extensive homology, about 25% of residues being identical in three regions that comprise about 70% of the molecules. Only minor similarities of uncertain significance were found among the complete amino acid sequences of the other cytokines. Although its evolutionary origin is uncertain, the homology around the N terminus may provide a structural marker for a group of cytokines active on the pluripotential hemopoietic stem cell and its derivatives.

L2 ANSWER 293 OF 302 MEDLINE
AN 86197728 MEDLINE
TI Development and characterization of antiserum to murine granulocyte-macrophage colony-stimulating factor.
AU Mochizuki D Y; Eisenman J R; Conlon P J; Park L S; Urdal D L
SO JOURNAL OF IMMUNOLOGY, (1986 May 15) 136 (10) 3706-9.
Journal code: IFB. ISSN: 0022-1767.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Abridged Index Medicus Journals; Priority Journals; Cancer Journals
EM 8608
AB The expression in yeast of a cDNA clone encoding murine granulocyte-macrophage colony-stimulating factor (GM-CSF) has made possible the purification of large quantities of this recombinant ***protein*** . Rabbits immunized with pure recombinant ***GM*** - ***CSF*** generated antibodies that were shown to be specific for both recombinant GM-CSF and GM-CSF isolated from natural sources. Other lymphokines, including IL 1 beta, IL 2, IL 3, and recombinant human GM-CSF did not react with the antiserum. The antiserum, together with recombinant GM-CSF that had been radiolabeled with 125I to high specific activity, formed the foundation for a rapid, sensitive, and quantitative radioimmunoassay specific for murine GM-CSF. Furthermore, the antiserum was found to inhibit the biologic activities of GM-CSF as measured in both a bone marrow proliferation assay and a colony assay, and thus should prove to be a useful reagent for dissecting the complex growth factor activities involved in murine hematopoiesis.

L2 ANSWER 294 OF 302 MEDLINE
AN 86179871 MEDLINE
TI Induction of macrophage tumoricidal activity by granulocyte-macrophage colony-stimulating factor.
AU Grabstein K H; Urdal D L; Tushinski R J; Mochizuki D Y; Price V L; Cantrell M A; Gillis S; Conlon P J
SO SCIENCE, (1986 Apr 25) 232 (4749) 506-8.
Journal code: UJ7. ISSN: 0036-8075.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
EM 8607
AB Monocytes are a subpopulation of peripheral blood leukocytes, which when appropriately activated by the regulatory hormones of the immune system, are capable of becoming macrophages--potent effector cells for immune response to tumors and parasites. A complementary DNA for the T lymphocyte-derived lymphokine, granulocyte-macrophage colony-stimulating factor (GM-CSF), has been cloned, and recombinant ***GM*** - ***CSF*** ***protein*** has been expressed in yeast and purified to homogeneity. This purified human recombinant GM-CSF stimulated peripheral blood monocytes in vitro to become cytotoxic for the malignant melanoma cell line A375. Another T cell-derived lymphokine, gamma-interferon (IFN-gamma), also stimulated peripheral blood monocytes to become tumoricidal against this malignant cell line. When IFN-gamma activates monocytes to become tumoricidal, additional stimulation by exogenously added lipopolysaccharide is required. No such exogenous signals were required for the activation of monocytes by GM-CSF.

L2 ANSWER 295 OF 302 MEDLINE
AN 86121386 MEDLINE
TI Pro-opiomelanocortin-related peptides in cerebrospinal fluid: a study of manic-depressive disorder.
AU Berrettini W H; Nurnberger J I Jr; Chan J S; Chrousos G P; Gaspar L; Gold P W; Seidah N G; Simmons-Alling S; Goldin L R; Chretien M; et al
SO PSYCHIATRY RESEARCH, (1985 Dec) 16 (4) 287-302.
Journal code: QC4. ISSN: 0165-1781.
CY Netherlands
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 8605
AB Five peptide fragments of pro-opiomelanocortin (alpha-melanocyte-stimulating hormone, beta-lipoprotin, adrenocorticotropic hormone, beta-endorphin, and the N-terminal fragment of pro-opiomelanocortin) were measured by radioimmunoassay in cerebrospinal fluid (CSF) and plasma from 31 normal volunteers and 26 euthymic lithium-treated bipolar patients (14 of whom provided a second CSF sample in the unmedicated state). With the exception of alpha-melanocyte-stimulating hormone, in the normal volunteers' CSF, levels of these peptides were highly correlated with one another, suggesting that: (1) some common regulatory factor may control the levels of these four ***peptides*** in CSF; and (2) ***CSF*** ***alpha*** -melanocyte-stimulating hormone is independently regulated from the other pro-opiomelanocortin products. Some of these correlations were absent in the patient groups, suggesting subtle alterations in pro-opiomelanocortin processing in manic-depressive illness. No effect of lithium on the CSF levels of these peptides was observed.

No group differences were found.

L2 ANSWER 296 OF 302 MEDLINE
AN 86078071 MEDLINE
TI Biosynthetic (recombinant) human granulocyte-macrophage colony-stimulating factor: effect on normal bone marrow and leukemia cell lines.
AU Tomonaga M; Golde D W; Gasson J C
NC CA32737
CA40163
CA30388
SO BLOOD, (1986 Jan) 67 (1) 31-6.
Journal code: A8G. ISSN: 0006-4971.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Abridged Index Medicus Journals; Priority Journals; Cancer Journals
EM 8604
AB To examine the biologic properties of the molecule encoded by the human gene for granulocyte-macrophage colony-stimulating factor (GM-CSF), we expressed the cloned complementary DNA (cDNA) in transfected monkey COS cells and purified the resultant ***protein*** . Purified biosynthetic human ***GM*** - ***CSF*** was added to cultures of normal hematopoietic progenitor cells in semisolid media, and the resulting colonies were characterized cytochemically. Non-adherent light-density bone marrow cells from healthy adult volunteers were maximally stimulated with GM-CSF (approximately 250 pmol/L, and four types of colonies were consistently identified by aspirating the individual colonies and staining with a triple stain for specific and nonspecific esterases and eosinophilic granules. Pure neutrophilic granulocyte (G), mixed granulocyte-macrophage (GM), pure macrophage (M), and pure eosinophil (EO) colonies were observed, the mean incidences on day 8 being 70%, 20%, 5%, and 5%, and on day 14, 7.5%, 16.6%, 50.9%, and 25.0%, respectively. In all types of colonies, complete maturation to segmented forms or typical macrophages was detected. GM-CSF did not enhance the growth of BFU-E from normal peripheral blood buffy coat cells in the simultaneous presence of erythropoietin alone or erythropoietin with purified erythroid-potentiating activity. GM-CSF stimulated HL-60 and KG-1 colony formation twofold and fivefold, respectively; consistent differentiation induction towards monocytic and eosinophilic lineages was observed in HL-60 but not in KG-1. These in vitro findings indicate that GM-CSF is a multilineage stimulator for progenitor cells of G, GM, M, and EO colonies.

L2 ANSWER 297 OF 302 MEDLINE
AN 86030235 MEDLINE
TI The structure and expression of the murine gene encoding granulocyte-macrophage colony stimulating factor: evidence for utilisation of alternative promoters.
AU Stanley E; Metcalf D; Sobieszczuk P; Gough N M; Dunn A R
NC CA25972
CA22556
SO EMBO JOURNAL, (1985 Oct) 4 (10) 2569-73.
Journal code: EMB. ISSN: 0261-4189.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
OS GENBANK-X03020
EM 8602
AB Two overlapping genomic clones containing the murine granulocyte-macrophage colony stimulating factor (GM-CSF) gene have been isolated. On the basis of transfection experiments, we have established that a 9-kb BamHI fragment from one of these recombinants encodes biologically active GM-CSF. As deduced from nucleotide sequence analysis, the GM-CSF gene comprises four exons encompassing 2.5 kb of genomic DNA. Primer extension analysis of GM-CSF mRNA identifies a transcriptional initiation site 35 bp upstream of a single translational initiation codon in-frame with the GM-CSF coding sequences and 28 bp downstream of a TATA promoter consensus sequence. Pre-GM-CSF molecules encoded by mRNAs originating from this promoter would include a hydrophobic leader sequence typical for a secreted protein. Intriguingly, sequences present at the 5' end of a GM-CSF cDNA clone previously isolated in our laboratory are not contained within either of the genomic clones and must therefore be transcribed from a promoter located at least 10 kb 5' of the main body of the gene. mRNAs transcribed from this alternative upstream promoter possess an additional initiating codon and potentially encode a pre- ***GM*** - ***CSF*** ***polypeptide*** with an atypical NH2-terminal leader peptide. Comparison of the nucleotide sequence of the GM-CSF gene with that of other haemopoietic growth factor genes has revealed a common decanucleotide (5'-GPuGPuTTPyCAPy-3') within their respective 5'-flanking regions which may be involved in their co-ordinate regulation.

L2 ANSWER 298 OF 302 MEDLINE
AN 85257511 MEDLINE
TI Specific binding of radioiodinated granulocyte-macrophage colony-stimulating factor to hemopoietic cells.
AU Walker F; Burgess A W
SO EMBO JOURNAL, (1985 Apr) 4 (4) 933-9.
Journal code: EMB. ISSN: 0261-4189.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 8511
AB The hemopoietic growth factor granulocyte-macrophage colony-stimulating factor, GM-CSF, specifically controls the production of granulocytes and macrophages. This report describes the binding of biologically-active 125I-labeled murine GM-CSF to a range of hemopoietic cells. Specific binding was restricted to murine cells and neither rat nor human bone marrow cells appeared to have surface receptors for 125I-labeled GM-CSF. 125I-Labeled GM-CSF only appeared to bind specifically to cells in the myelomonocytic lineage. The binding of 125I-labeled GM-CSF to both bone marrow cells and WEHI-3B(D+) was rapid (50% maximum binding was attained within 5 min at both 20 degrees C and 37 degrees C). Unlabeled ***GM*** - ***CSF*** was the only ***polypeptide*** hormone which completely inhibited the binding of 125I-labeled GM-CSF to bone marrow cells, however, multi-CSF (also called IL-3) and G-CSF partially reduced the binding of 125I-labeled GM-CSF to bone marrow cells. Interestingly, the binding of 125I-labeled GM-CSF to a myelomonocytic cell line, WEHI-3B(D+), was inhibited by unlabeled GM-CSF but not by multi-CSF or G-CSF. Scatchard analysis of the binding of 125I-labeled GM-CSF to WEHI-3B(D+) cells, bone marrow cells and peritoneal neutrophils indicated that there were two classes of binding sites: one of high affinity (Kd1 = 20 pM) and one of low affinity (Kd2 = 0.8-1.2 nM). Multi-CSF only inhibited the binding of 125I-labeled GM-CSF to the high affinity receptor on bone marrow cells: this inhibition appeared to be a result of down regulation or modification of the GM-CSF receptor.(ABSTRACT TRUNCATED AT 250 WORDS)

L2 ANSWER 299 OF 302 MEDLINE
AN 85228842 MEDLINE
TI ***CSF*** ***alpha*** 2-macroglobulin and C-reactive ***protein*** as aids to rapid diagnosis of acute bacterial meningitis.
AU Virji M A; Diven W F; Kelly R H
SO CLINICA CHIMICA ACTA, (1985 May 15) 148 (1) 31-7.
Journal code: DCC. ISSN: 0009-8981.
CY Netherlands
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 8510
AB alpha 2-Macroglobulin (AMG) and C-reactive protein (CRP) levels in cerebrospinal fluid (CSF) of patients with bacterial and aseptic meningitis have been analyzed by a rate nephelometric method to determine if these acute phase proteins can aid in differentiation of bacterial from aseptic meningitis. The mean CSF concentrations of AMG and CRP were 15 and 3.5 times greater, respectively, in the bacterial compared to the aseptic meningitis group. Also, the range of AMG levels showed minimal overlap between the two groups. The elevated levels of the proteins persisted after CSF cultures became negative. Quantitation of specific acute phase proteins in CSF may assist the differentiation of bacterial from aseptic meningitis.

L2 ANSWER 300 OF 302 MEDLINE
AN 84220341 MEDLINE
TI [Markers of brain tumors].
I marker dei tumori cerebrali.
AU Fumagalli R; Pezzotta S; Bernini F; Racagni G
SO MINERVA MEDICA, (1984 May 19) 75 (21) 1271-8.
Journal code: N6M. ISSN: 0026-4806.
CY Italy
DT Journal; Article; (JOURNAL ARTICLE)
LA Italian
FS Priority Journals; Cancer Journals

EM 8409

AB Biological markers of tumors are compounds or enzymatic activities measurable in body fluids. Their presence or concentration must be linked to tumoral growth. The markers of the central nervous system tumors are detected in ***CSF*** . ***Alpha*** -feto-***protein*** , carcinoembryonic antigen, human chorionic gonadotropin, adenohypophyseal peptide hormones, enzymes, etc., have found some application in the early diagnosis of leptomeningeal metastasis. Other applications involve the early detection and recurrency of primary brain tumors, as well as the evaluation of efficacy of their therapy. The tests based on the CSF content of desmosterol and polyamines have been studied extensively. Their rationale is discussed and specificity, sensitivity, efficiency and predictive value are considered. Experimental results concerning a new possible biochemical marker, based on CSF concentration of cyclic adenosine monophosphate, are reported.

L2 ANSWER 301 OF 302 MEDLINE

AN 84212822 MEDLINE

TI Granulocyte macrophage-colony stimulating factor stimulates the synthesis of membrane and nuclear proteins in murine neutrophils.

AU Stanley I J; Burgess A W

NC CA-22556

SO JOURNAL OF CELLULAR BIOCHEMISTRY, (1983) 23 (1-4) 241-58. Journal code: HNF. ISSN: 0730-2312.

CY United States

DT Journal; Article; (JOURNAL ARTICLE)

LA English

FS Priority Journals

EM 8409

AB The effect of granulocyte macrophage-colony stimulating factor (GM-CSF), a well-characterized hemopoietic regulator, on protein synthesis in murine bone marrow neutrophils is described. Bone marrow neutrophils in excess of 95% purity were obtained by fluorescence-activated cell sorting. While GM-CSF did not appear to slow the rate of dying of peritoneal exudate neutorphils or thymus cells, the viability of bone marrow neutrophils after 17 hr was enhanced (40%) by GM-CSF. GM-CFS had no effect on total 35S-methionine incorporation by thymocytes or peritoneal exudate neutrophils over a 17-hr incubation period; however, bone marrow neutrophils showed increased incorporation (approximately 10%) at all times between 5-17 hr. As viability and 35S-methionine incorporation of bone marrow neutrophils at 5 hr were minimally affected by GM-CSF, this time point was chosen to study the effect of ***GM*** - ***CSF*** on the synthesis of particular ***proteins*** . Two-dimensional polyacrylamide gels of 35S-methionine-labelled lysates were prepared from whole cells, isolated nuclei, and membranes. Quantitative analysis of the fluorograms obtained from the two-dimensional electropherograms by a computer-linked optical data digitiser indicated that out of a total of 180 proteins, the amount of label contained in 11 proteins was significantly higher in the presence of ***GM*** - ***CSF*** , while three ***proteins*** , apparently of cytoplasmic origin, contained less label than control cells. Eight of these proteins were identified as nuclear, and one was membrane derived. Attempts have been made to identify some of the inducible proteins and to correlate results with other studies of normal hemopoietic and leukemic cells. The significance and multiple functions of GM-CSF in hemopoiesis are discussed.

L2 ANSWER 302 OF 302 MEDLINE

AN 80228058 MEDLINE

TI Secretion and partial degradation of granulocyte-macrophage colony-stimulating factor (GM-CSF) of mouse L-P3 cells.

AU Tsuneoka K; Shikita M

SO JOURNAL OF CELLULAR PHYSIOLOGY, (1980 Mar) 102 (3) 333-41. Journal code: HNB. ISSN: 0021-9541.

CY United States

DT Journal; Article; (JOURNAL ARTICLE)

LA English

FS Priority Journals

EM 8011

AB Secretion of a granulocyte-macrophage colony-stimulating factor (GM-CSF) was accomplished by L-P3 cells in culture with a serum-free medium. Cell proliferation per se was not requisite for the production of GM-CSF; the cells continued secreting GM-CSF even after their growth had been suspended. The amount of GM-CSF accumulated in the conditioned medium was reasonably accounted by the daily rate of production, and the addition of a proteinase inhibitor such as leupeptin and pepstatin did not result in greater accumulation of GM-CSF in the culture. It is thus postulated that there is no significant proteolytic inactivation of the secreted GM-CSF in the culture. However, when partially purified GM-CSF preparation was chromatographed on a gel-filtration column in the presence of 0.1% Triton X-100, a derivative of the GM-CSF was yielded which had been diminished in the molecular weight and altered in the isoelectric point. On the other hand, when leupeptin was included in the solution during production and isolation of the factor, the yielded GM-CSF did not manifest such a detergent-induced transformation and maintained its isoelectric point at pH 3.5. It is thus assumed that, in the presence of the detergent, ***GM*** - ***CSF*** suffers deterioration by an endogenous ***proteinase*** and releases a sialoglycopeptide fragment without loosing its colony-stimulating activity.